(54) Title: METHODS FOR DIAGNOSING AND TREATING HEART DISEASE

(57) Abstract: The invention provides methods of diagnosing heart disease, such as heart failure, screening methods for identifying
compounds that can be used to treat or to prevent heart disease, and methods of using these compounds to treat or to prevent heart
disease. The invention also provides animal model systems for carrying out the screening methods.

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METHODS FOR DIAGNOSING AND TREATING HEART DISEASE

Field of the Invention

5   This invention relates to methods for diagnosing and treating heart disease.

Background of the Invention

Heart disease is a general term used to describe many different heart conditions. For example, coronary artery disease, which is the most common heart disease, is characterized by constriction or narrowing of the arteries supplying the heart with oxygen-rich blood, and can lead to myocardial infarction, which is the death of a portion of the heart muscle. Heart failure is a condition resulting from the inability of the heart to pump an adequate amount of blood through the body. Heart failure is not a sudden, abrupt stop of heart activity, but, rather, typically develops slowly over many years, as the heart gradually loses its ability to pump blood efficiently. Risk factors for heart failure include coronary artery disease, hypertension, valvular heart disease, cardiomyopathy, disease of the heart muscle, obesity, diabetes, and a family history of heart failure.

Summary of the Invention

The invention provides diagnostic, drug screening, and therapeutic methods based on the observation that mutation of the *titin* gene leads to a phenotype in zebrafish that is similar to mammalian heart failure.

In one aspect, the invention provides a method of determining whether a test subject (*e.g.*, a mammal, such as a human) has, or is at risk of developing, a titin-related disease or condition (*e.g.*, heart failure). This method involves analyzing a nucleic acid molecule of a sample from the

5 test subject to determine whether the test subject has a mutation (for example, a mutation in a cardiac-specific exon, such as the N2B exon; *e.g.*, the *pickwick* mutation; see below) in a *titin* gene. The presence of such a mutation is an indication that the test subject has, or is at risk of developing, a titin-related disease. This method can further involve using

10 nucleic acid molecule primers specific for the *titin* gene for nucleic acid molecule amplification of the *titin* gene by the polymerase chain reaction, or sequencing *titin* nucleic acid molecules from the test subject.

In another aspect, the invention provides a screening method for identifying a compound that can be used to treat or to prevent heart failure.

15 This method involves contacting an organism (*e.g.*, a zebrafish) having a *titin* mutation (for example, a mutation in a cardiac-specific exon, such as the N2B exon; *e.g.*, the *pickwick* mutation) and a phenotype characteristic of heart failure with the compound, and determining the effect of the compound on the phenotype. Detection of an improvement in the

20 phenotype indicates the identification of a compound that can be used to treat or to prevent heart failure.

In another aspect, the invention provides a method of treating or preventing heart disease, such as heart failure, in a patient. This method involves administering to the patient a compound identified using the

25 screening method described above. A patient treated using this method can have a mutation in the *titin* gene.

In a further aspect, the invention provides a non-human animal (*e.g.*, a zebrafish or a mouse) that has a mutation in a *titin* gene. The

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mutation can be, for example, in a cardiac-specific exon of the *titin* gene, such as the N2B exon, and can result in production of a truncated titin product, for example, by the introduction of a stop codon.

By "polypeptide" or "polypeptide fragment" is meant a chain of
5 two or more amino acids, regardless of any post-translational modification (*e.g.*, glycosylation or phosphorylation), constituting all or part of a naturally or non-naturally occurring polypeptide. By "post-translational modification" is meant any change to a polypeptide or polypeptide fragment during or after synthesis. Post-translational modifications can be
10 produced naturally (such as during synthesis within a cell) or generated artificially (such as by recombinant or chemical means). A "protein" can be made up of one or more polypeptides.

By "titin," "titin protein," or "titin polypeptide" is meant a polypeptide that has at least 45%, preferably at least 60%, more preferably
15 at least 75%, and most preferably at least 90% amino acid sequence identity to the sequence of the human (see below) or the zebrafish titin polypeptides. Polypeptide products from splice variants of *titin* gene sequences and *titin* genes containing mutations are also included in this definition. A titin polypeptide as defined herein plays a role in heart
20 development, modeling, structure, and contractility. It can be used as a marker of heart disease, such as heart failure.

By a "*titin* nucleic acid molecule" is meant a nucleic acid molecule, such as a genomic DNA, cDNA, or RNA (*e.g.*, mRNA) molecule, that encodes titin, a titin protein, a titin polypeptide, or a portion thereof, as
25 defined above.

The term "identity" is used herein to describe the relationship of the sequence of a particular nucleic acid molecule or polypeptide to the sequence of a reference molecule of the same type. For example, if a

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polypeptide or nucleic acid molecule has the same amino acid or
nucleotide residue at a given position, compared to a reference molecule to
which it is aligned, there is said to be "identity" at that position. The level
of sequence identity of a nucleic acid molecule or a polypeptide to a

5   reference molecule is typically measured using sequence analysis software
with the default parameters specified therein, such as the introduction of
gaps to achieve an optimal alignment (e.g., Sequence Analysis Software
Package of the Genetics Computer Group, University of Wisconsin
Biotechnology Center, 1710 University Avenue, Madison, WI 53705,

10 BLAST, or PILEUP/PRETTYBOX programs). These software programs
match identical or similar sequences by assigning degrees of identity to
various substitutions, deletions, or other modifications. Conservative
substitutions typically include substitutions within the following groups:
glycine, alanine, valine, isoleucine, and leucine; aspartic acid, glutamic

15 acid, asparagine, and glutamine; serine and threonine; lysine and arginine;
and phenylalanine and tyrosine.

A nucleic acid molecule or polypeptide is said to be "substantially
identical" to a reference molecule if it exhibits, over its entire length, at
least 51%, preferably at least 55%, 60%, or 65%, and most preferably

20 75%, 85%, 90%, or 95% identity to the sequence of the reference
molecule. For polypeptides, the length of comparison sequences is at least
16 amino acids, preferably at least 20 amino acids, more preferably at least
25 amino acids, and most preferably at least 35 amino acids. For nucleic
acid molecules, the length of comparison sequences is at least 50

25 nucleotides, preferably at least 60 nucleotides, more preferably at least 75
nucleotides, and most preferably at least 110 nucleotides.

A *titin* nucleic acid molecule or titin polypeptide is "analyzed" or
subject to "analysis" if a test procedure is carried out on it that allows the

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determination of its biological activity or whether it is wild type or
mutated. For example, one can analyze the *titin* genes of an animal (*e.g.*, a
human or a zebrafish) by amplifying genomic DNA of the animal using
the polymerase chain reaction, and then determining whether the amplified

5 DNA contains a mutation, for example, the *pickwick* mutation, by, *e.g.*,
nucleotide sequence or restriction fragment analysis.

By "probe" or "primer" is meant a single-stranded DNA or RNA
molecule of defined sequence that can base pair to a second DNA or RNA
molecule that contains a complementary sequence ("target"). The stability

10 of the resulting hybrid depends upon the extent of the base pairing that
occurs. This stability is affected by parameters such as the degree of
complementarity between the probe and target molecule, and the degree of
stringency of the hybridization conditions. The degree of hybridization
stringency is affected by parameters such as the temperature, salt

15 concentration, and concentration of organic molecules, such as formamide,
and is determined by methods that are well known to those skilled in the
art. Probes or primers specific for *titin* nucleic acid molecules, preferably,
have greater than 45% sequence identity, more preferably at least 55-75%
sequence identity, still more preferably at least 75-85% sequence identity,

20 yet more preferably at least 85-99% sequence identity, and most
preferably 100% sequence identity to the sequences of human (see below)
or zebrafish *titin*.

Probes can be detectably-labeled, either radioactively or non-
radioactively, by methods that are well-known to those skilled in the art.

25 Probes can be used for methods involving nucleic acid hybridization, such
as nucleic acid sequencing, nucleic acid amplification by the polymerase
chain reaction, single stranded conformational polymorphism (SSCP)
analysis, restriction fragment polymorphism (RFLP) analysis, Southern

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hybridization, northern hybridization, *in situ* hybridization, electrophoretic

mobility shift assay (EMSA), and other methods that are well known to

those skilled in the art.

A molecule, *e.g.*, an oligonucleotide probe or primer, a gene or

5   fragment thereof, a cDNA molecule, a polypeptide, or an antibody, can be

said to be "detectably-labeled" if it is marked in such a way that its

presence can be directly identified in a sample. Methods for detectably-

labeling molecules are well known in the art and include, without

limitation, radioactive labeling (*e.g.*, with an isotope, such as ^{32}P or ^{35}S)

10   and nonradioactive labeling (*e.g.*, with a fluorescent label, such as

fluorescein).

By a "substantially pure polypeptide" is meant a polypeptide (or a

fragment thereof) that has been separated from proteins and organic

molecules that naturally accompany it. Typically, a polypeptide is

15   substantially pure when it is at least 60%, by weight, free from the proteins

and naturally-occurring organic molecules with which it is naturally

associated. Preferably, the polypeptide is a titin polypeptide that is at least

75%, more preferably at least 90%, and most preferably at least 99%, by

weight, pure. A substantially pure titin polypeptide can be obtained, for

20   example, by extraction from a natural source (*e.g.*, isolated heart tissue),

by expression of a recombinant nucleic acid molecule encoding a titin

polypeptide, or by chemical synthesis. Purity can be measured by any

appropriate method, *e.g.*, by column chromatography, polyacrylamide gel

electrophoresis, or HPLC analysis.

25   A polypeptide is substantially free of naturally associated

components when it is separated from those proteins and organic

molecules that accompany it in its natural state. Thus, a protein that is

chemically synthesized or produced in a cellular system different from the

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cell in which it is naturally produced is substantially free from its naturally
associated components. Accordingly, substantially pure polypeptides not
only include those derived from eukaryotic organisms, but also those
synthesized in *E. coli* or other prokaryotes.

5   An antibody is said to "specifically bind" to a polypeptide if it
recognizes and binds to the polypeptide (*e.g.*, a titin polypeptide), but does
not substantially recognize and bind to other molecules (*e.g.*, non-titin
related polypeptides) in a sample, *e.g.*, a biological sample that naturally
includes the polypeptide.

10   By "high stringency conditions" is meant conditions that allow
hybridization comparable with the hybridization that occurs using a DNA
probe of at least 500 nucleotides in length, in a buffer containing 0.5 M
$NaHPO_4$, pH 7.2, 7% SDS, 1 mM EDTA, and 1% BSA (fraction V), at a
temperature of 65°C, or a buffer containing 48% formamide, 4.8 x SSC,

15   0.2 M Tris-Cl, pH 7.6, 1 x Denhardt's solution, 10% dextran sulfate, and
0.1% SDS, at a temperature of 42°C. (These are typical conditions for
high stringency northern or Southern hybridizations.) High stringency
hybridization is also relied upon for the success of numerous techniques
routinely performed by molecular biologists, such as high stringency PCR,

20   DNA sequencing, single strand conformational polymorphism analysis,
and *in situ* hybridization. In contrast to northern and Southern
hybridizations, these techniques are usually performed with relatively
short probes (*e.g.*, usually 16 nucleotides or longer for PCR or sequencing
and 40 nucleotides or longer for *in situ* hybridization). The high

25   stringency conditions used in these techniques are well known to those
skilled in the art of molecular biology, and examples of them can be

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found, for example, in Ausubel *et al.*, *Current Protocols in Molecular Biology*, John Wiley & Sons, New York, NY, 1998, which is hereby incorporated by reference.

By "sample" is meant a tissue biopsy, amniotic fluid, cell, blood,
5   serum, urine, stool, or other specimen obtained from a patient or test
subject. The sample can be analyzed to detect a mutation in a *titin* gene,
or expression levels of a *titin* gene, by methods that are known in the art.
For example, methods such as sequencing, single-strand conformational
polymorphism (SSCP) analysis, or restriction fragment length
10 polymorphism (RFLP) analysis of PCR products derived from a patient
sample can be used to detect a mutation in a *titin* gene; ELISA can be used
to measure levels of titin polypeptide; and PCR can be used to measure the
level of a *titin* nucleic acid molecule.

By "titin-related disease" or "titin-related condition" is meant a
15 disease or condition that results from inappropriately high or low
expression of a *titin* gene, or a mutation in a *titin* gene that alters the
biological activity of a *titin* nucleic acid molecule or polypeptide. Titin-
related diseases and conditions can arise in any tissue in which titin is
expressed during prenatal or post-natal life. Titin-related diseases and
20 conditions can include heart diseases, such as heart failure. Specific
examples of different types of heart failure are provided below.

The invention provides several advantages. For example, using the
diagnostic methods of the invention, it is possible to detect an increased
likelihood of heart disease, such as heart failure, in a patient, so that
25 appropriate intervention can be instituted before any symptoms occur.
This may be useful, for example, with patients in high-risk groups for
heart failure (see above). Also, the diagnostic methods of the invention
facilitate determination of the etiology of an existing heart condition, such

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as heart failure, in a patient, so that an appropriate approach to treatment can be selected. In addition, the screening methods of the invention can be used to identify compounds that can be used to treat or to prevent heart conditions, such as heart failure.

5   Other features and advantages of the invention will be apparent from the following detailed description and the claims.

Brief Description of the Drawing

Fig. 1 is a schematic representation of the domain structure of the human titin filament. The nucleotide and amino acid sequences of human 10 titin are provided in SEQ ID NOs:1 and 2, respectively. The modular architecture of cardiac titin as predicted by its full-length cDNA is shown.

A total of 244 copies of 100 residue repeats, as indicated by vertical rectangles, are contained in the molecule. One hundred and twelve of these belong to the Ig domain, and 132 belong to the FN3 superfamily. 15 The titin kinase domain, as well as the PEVK element N2-B 163-residue variant are also shown. Within the A-band , the D-zone contains six tandem repeats of the seven domains shown (A1 through A42), and the C-zone contains 11 tandem repeats of the 11 domains shown (A43 through A163). The positions of the tandemly repeated RMSP and VKSP motifs 20 in the Z-disc and M-line region are also shown

Detailed Description

The invention provides methods of diagnosing heart disease, screening methods for identifying compounds that can be used to treat or to prevent heart disease, and methods of treating or preventing heart

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disease using these compounds. The invention also provides animal
model systems that can be used in the screening methods of the invention.

In particular, we have discovered that a mutation (the *pickwick*
mutation) in the *titin* gene is associated with heart disease, such as heart

5   failure. Titin, which is also known as "connectin," is the largest known
single-chain protein, having a molecular weight of about 3,000 kDa. Titin
is a structural protein, and plays a central role in the assembly and
elasticity of vertebrate skeletal and cardiac muscle. Thus, the diagnostic
methods of the invention involve detection of mutations in the *titin* gene,

10 while the compound identification methods of the invention involve
screening for compounds that affect the phenotype of *titin* mutants or other
models of heart disease, such as heart failure. Compounds identified in
this manner can be used in methods to treat or to prevent heart disease
(*e.g.*, heart failure). The diagnostic, screening, and therapeutic methods of

15 the invention, as well as the animal model systems of the invention, are
described further, as follows.

Diagnostic Methods

Titin nucleic acid molecules, polypeptides, and antibodies can be
used in methods to diagnose or to monitor diseases and conditions

20 involving mutations in, or inappropriate expression of, *titin* genes. As
discussed further below, the *pickwick* mutation in zebrafish, which is
present in the *titin* gene, is characterized by a phenotype that is similar to
that of heart failure in humans. Thus, detection of abnormalities in *titin*
genes or their expression can be used in methods to diagnose, or to

25 monitor treatment or development of, human heart disease, such as heart
failure. For use as references, the human cardiac *titin* cDNA sequence can
be found at:

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http://www.embl-heidelberg.de/ExternalInfo/Titin/cardiacseq.html (SEQ ID NO:1), while the corresponding protein sequence can be found at: http://www.embl-heidelberg.de/ExternalInfo/Titin/cardiacpep.html (SEQ ID NO:2).

5   As noted above, the diagnostic methods of the invention can be used, for example, with patients that have heart failure, in an effort to determine its etiology and, thus, to facilitate selection of an appropriate course of treatment. The diagnostic methods can also be used with patients that have not yet developed heart failure, but who are at risk of

10   developing such a disease, or with patients that are at an early stage of developing such a disease. Also, the diagnostic methods of the invention can be used in prenatal genetic screening, for example, to identify parents who may be carriers of a recessive *titin* mutation.

Examples of heart failure that can be diagnosed (and treated) using

15   the methods of the invention include congestive heart failure, which is characterized by fluid in the lungs or body, resulting from failure of the heart in acting as a pump; right sided heart failure (right ventricular), which is characterized by failure of the pumping action of the right ventricle, resulting in swelling of the body, especially the legs and

20   abdomen; left sided heart failure (left ventricular), which is caused by failure of the pumping action of the left side of the heart, resulting in congestion of the lungs; forward heart failure, which is characterized by the inability of the heart to pump blood forward at a sufficient rate to meet the oxygen needs of the body at rest or during exercise; backward heart

25   failure, which is characterized by the ability of the heart to meet the needs of the body only if heart filling pressures are abnormally high; low-output,

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which is characterized by failure to maintain blood output; and

high-output, which is characterized by heart failure symptoms, even when

cardiac output is high.

Titin may also play a role in cardiovascular diseases other than

5   heart failure, such as coronary artery disease or conditions associated with

valve formation defects, and, thus, detection of abnormalities in *titin* genes

or their expression can be used in methods to diagnose and monitor these

conditions as well. The methods of the invention can be used to diagnose

(or to treat) the disorders described herein in any mammal, for example,

10 humans, domestic pets, or livestock.

Titin abnormalities that can be detected using the diagnostic

methods of the invention include those characterized by, for example, (i)

abnormal titin polypeptides, (ii) *titin* genes containing mutations that result

in the production of such polypeptides, and (iii) *titin* mutations that result

15 in production of abnormal amounts of titin. Detection of such

abnormalities, thus, can be used in methods to diagnose human heart

disease, such as heart failure. Exemplary of the *titin* mutations that can be

detected using the methods of the invention is the *pickwick* mutation (see

below).

20   Detection of *titin* mutations can be carried out using any diagnostic

technique. For example, a biological sample obtained from a patient can

be analyzed for one or more mutations in *titin* nucleic acid molecules (*e.g.,*

the *pickwick* mutation) using a mismatch detection approach. Generally,

this approach involves polymerase chain reaction (PCR) amplification of

25 nucleic acid molecules from a patient sample, followed by identification of

a mutation (*i.e.,* a mismatch) by detection of altered hybridization, aberrant

electrophoretic gel migration, binding, or cleavage mediated by mismatch

binding proteins, or by direct nucleic acid molecule sequencing. Any of

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these techniques can be used to facilitate detection of mutant *titin* genes, and each is well known in the art. Examples of these techniques are described by Orita *et al.* (Proc. Natl. Acad. Sci. U.S.A. 86:2766-2770, 1989) and Sheffield *et al.* (Proc. Natl. Acad. Sci. U.S.A. 86:232-236,

5 1989).

Mutation detection assays also provide an opportunity to diagnose a titin-mediated predisposition to heart disease before the onset of symptoms. For example, a patient heterozygous for a *titin* mutation that suppresses normal titin biological activity or expression may show no

10 clinical symptoms of a titin-related disease, and yet possess a higher than normal probability of developing heart disease, such as heart failure. Given such a diagnosis, a patient can take precautions to minimize exposure to adverse environmental factors, and can carefully monitor their medical condition, for example, through frequent physical examinations.

15 As mentioned above, this type of diagnostic approach can also be used to detect *titin* mutations in prenatal screens.

The *titin* diagnostic assays described above can be carried out using any biological sample (for example, a muscle tissue sample) in which titin is normally expressed. Because of the limited number of tissues in which

20 titin is expressed, as well as the relative difficulties involved in obtaining samples of these tissues, it may be preferable to detect mutant *titin* genes in another, more easily obtained sample type, such as blood or amniotic fluid samples using, for example, mismatch detection techniques. Preferably, the DNA in such a sample is subjected to PCR amplification

25 prior to analysis.

Levels of titin expression in a patient sample can be determined by using any of a number of standard techniques that are well known in the art. For example, titin expression in a biological sample (*e.g.*, a blood or

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tissue sample, or amniotic fluid) from a patient can be monitored by standard northern blot analysis or by quantitative PCR (see, *e.g.*, Ausubel *et al.*, *supra*; *PCR Technology: Principles and Applications for DNA Amplification*, H.A. Ehrlich, Ed., Stockton Press, NY; Yap *et al.*, Nucl.

5 Acids. Res. 19:4294, 1991).

In yet another diagnostic approach of the invention, an immunoassay is used to detect or to monitor titin protein levels in a biological sample. Titin-specific polyclonal or monoclonal antibodies can be used in any standard immunoassay format (*e.g.*, ELISA, Western blot,

10 or RIA; see, *e.g.*, Ausubel *et al.*, *supra*) to measure titin polypeptide levels. These levels are compared to wild-type titin levels. For example, a decrease in titin production may be indicative of a condition or a predisposition to a condition involving insufficient titin biological activity.

Immunohistochemical techniques can also be utilized for titin

15 detection. For example, a tissue sample can be obtained from a patient, sectioned, and stained for the presence of titin using an anti-titin antibody and any standard detection system (*e.g.*, one that includes a secondary antibody conjugated to horseradish peroxidase). General guidance regarding such techniques can be found in, *e.g.*, Bancroft *et al.*, *Theory*

20 *and Practice of Histological Techniques*, Churchill Livingstone, 1982, and in Ausubel *et al.*, *supra*.

Identification of Molecules That Can Be Used to Treat or to Prevent Heart Failure

Identification of a mutation in *titin* as resulting in a phenotype that

25 is related to heart failure facilitates the identification of molecules (*e.g.*, small organic molecules, peptides, or nucleic acid molecules) that can be

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used to treat or to prevent heart failure. The effects of candidate

compounds on heart failure can be investigated using, for example, the

zebrafish system. The zebrafish, *Danio rerio*, is a convenient organism to

use in genetic analysis of vascular development. In addition to its short

5   generation time and fecundity, it has an accessible and transparent embryo,

allowing direct observation of blood vessel function from the earliest

stages. As discussed further below, zebrafish and other animals having

mutations in the *titin* gene, which can be used in these methods, are also

included in the invention.

10   In one example of the screening methods of the invention, a

zebrafish having a mutation in the *titin* gene (*e.g.*, a zebrafish having the

pickwick mutation; see below) is contacted with a candidate compound,

and the effect of the compound on the development of a heart abnormality

that is characteristic of heart failure, or on the status of such an existing

15   heart abnormality, is monitored, relative to an untreated, identically mutant

control. As discussed further below, zebrafish having the *pickwick*

mutation are characterized by, for example, reduction of peak systolic

pressures, stretched and thin myocardium, excess cardiac jelly, absent A-V

cushions, and an obstructed ventricular outflow tract. Thus, these

20   characteristics (in addition to other characteristics of heart failure) can be

monitored using the screening methods of the invention.

       After a compound has been shown to have a desired effect in the

zebrafish system, it can be tested in other models of heart disease, for

example, in mice or other animals having a mutation in the *titin* gene.

25   Alternatively, testing in such animal model systems can be carried out in

the absence of zebrafish testing.

       Candidate compounds can be purified (or substantially purified)

molecules or can be one component of a mixture of compounds (*e.g.*, an

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extract or supernatant obtained from cells; Ausubel *et al.*, *supra*). In a

mixed compound assay, the effect on a phenotype of heart failure is tested

against progressively smaller subsets of the candidate compound pool

(*e.g.*, produced by standard purification techniques, *e.g.*, HPLC or FPLC)

5   until a single compound or minimal compound mixture is demonstrated to

have the desired effect.

Test compounds that can be screened in the methods described

above can be chemicals that are naturally occurring or artificially derived.

Such compounds can include, for example, polypeptides, synthesized

10   organic molecules, naturally occurring organic molecules, nucleic acid

molecules, and components thereof. Candidate compound can be found,

for example, in a cell extract, mammalian serum, or growth medium in

which mammalian cells have been cultured.

In general, novel drugs for prevention or treatment of mutant titin-

15   related heart diseases can be identified from large libraries of both natural

products, synthetic (or semi-synthetic) extracts, and chemical libraries

using methods that are well known in the art. Those skilled in the field of

drug discovery and development will understand that the precise source of

test extracts or compounds is not critical to the screening methods of the

20   invention. Accordingly, virtually any number of chemical extracts or

compounds can be screened using these methods. Examples of such

extracts or compounds include, but are not limited to, plant-, fungal-,

prokaryotic-, or animal-based extracts, fermentation broths, and synthetic

compounds, as well as modifications of existing compounds.

25   Numerous methods are also available for generating random or

directed synthesis (*e.g.*, semi-synthesis or total synthesis) of any number

of chemical compounds, including, but not limited to, saccharide-, lipid-,

peptide-, and nucleic acid molecule-based compounds. Synthetic

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compound libraries are commercially available from Brandon Associates (Merrimack, NH) and Aldrich Chemical (Milwaukee, WI). Alternatively, libraries of natural compounds in the form of bacterial, fungal, plant, and animal extracts are commercially available from a number of sources,

5   including Biotics (Sussex, UK), Xenova (Slough, UK), Harbor Branch Oceanographic Institute (Ft. Pierce, FL), and PharmaMar, U.S.A. (Cambridge, MA). In addition, natural and synthetically produced libraries can be produced, if desired, according to methods known in the art, e.g., by standard extraction and fractionation. Furthermore, if desired,

10   any library or compound can be readily modified using standard chemical, physical, or biochemical methods.

        In addition, those skilled in the art of drug discovery and development readily understand that methods for dereplication (e.g., taxonomic dereplication, biological dereplication, and chemical

15   dereplication, or any combination thereof) or the elimination of replicates or repeats of materials already known for their therapeutic activities for heart failure can be employed whenever possible.

        When a crude extract is found to have an effect on the development or persistence of heart failure, further fractionation of the positive lead

20   extract can be carried out to isolate chemical constituents responsible for the observed effect. Thus, the goal of the extraction, fractionation, and purification process is the careful characterization and identification of a chemical entity within the crude extract having a desired activity. The same assays described herein for the detection of activities in mixtures of

25   compounds can be used to purify the active component and to test derivatives of these compounds. Methods of fractionation and purification of such heterogeneous extracts are well known in the art. If desired,

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compounds shown to be useful agents for treatment can be chemically modified according to methods known in the art.

Treatment or Prevention of Heart Failure

Compounds identified using the screening methods described above
5   can be used to treat patients that have or are at risk of developing heart disease, such as heart failure. Such treatment may be required only for a short period of time, or may, in some form, be required throughout a patient's lifetime. Any continued need for treatment, however, can be determined using, for example, the diagnostic methods described above.
10 In considering various therapies, it is understood that such therapies are, preferably, targeted to the affected or potentially affected organ, that is, the heart.

Treatment or prevention of diseases resulting from a mutated *titin* gene can be accomplished, for example, by modulating the function of a
15 mutant titin protein, delivering normal titin protein to the appropriate cells, altering the levels of normal or mutant titin protein, replacing a mutant *titin* gene with a normal *titin* gene or, administering a normal *titin* gene. It is also possible to correct a *titin* defect by modifying the physiological pathway (*e.g.*, a signal transduction pathway) in which the titin protein
20 participates.

In a patient diagnosed as heterozygous for a *titin* mutation, or as susceptible to *titin* mutations or aberrant titin expression (even if those mutations or expression patterns do not yet result in alterations in titin expression or biological activity), any of the above-described therapies can
25 be administered before the occurrence of the disease phenotype. In particular, compounds shown to modulate titin expression or to have an

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effect on the phenotype of *titin* mutants can be administered to patients diagnosed with potential or actual heart disease by any standard dosage and route of administration.

Any appropriate route of administration can be employed to
5   administer a compound found to be effective in treating or preventing heart failure, according to the invention. For example, administration can be parenteral, intravenous, intra-arterial, subcutaneous, intramuscular, intraventricular, intracapsular, intraspinal, intracisternal, intraperitoneal, intranasal, aerosol, or oral. However, as noted above, preferably, the
10   administration is local to the afflicted tissue, that is, the heart. Therapeutic formulations can be in the form of liquid solutions or suspensions; for oral administration, formulations can be in the form of tablets or capsules; and for intranasal formulations, in the form of powders, nasal drops, or aerosols.

15   A therapeutic compound of the invention can be administered within a pharmaceutically acceptable diluent, carrier, or excipient, in unit dosage form. Administration can begin before or after the patient is symptomatic. Methods that are well known in the art for making formulations are found, for example, in *Remington's Pharmaceutical*
20   *Sciences*, (18th edition), ed. A. Gennaro, 1990, Mack Publishing Company, Easton, PA. Formulations for parenteral administration can, for example, contain excipients; sterile water; or saline; polyalkylene glycols, such as polyethylene glycol; oils of vegetable origin; or hydrogenated napthalenes. Biocompatible, biodegradable lactide polymer, lactide/glycolide
25   copolymer, or polyoxyethylene-polyoxypropylene copolymers can be used to control the release of the compounds. Other potentially useful parenteral delivery systems for compounds identified using the methods of the invention include ethylene-vinyl acetate copolymer particles, osmotic

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pumps, implantable infusion systems, and liposomes. Formulations for inhalation can contain excipients, for example, lactose, or can be aqueous solutions containing, for example, polyoxyethylene-9-lauryl ether, glycocholate, and deoxycholate, or can be oily solutions for administration

5   in the form of nasal drops, or as a gel.

Titin nucleic acid molecules and polypeptides can also be used in tissue engineering, for example, in the manufacture of artificial or partially artificial hearts. As mentioned above, titin plays a role in cardiovascular elasticity, integrity, and contractility. Thus, a titin nucleic acid molecule

10   or polypeptide, as described above, can be used to impart such characteristics on an artificial or partially artificial heart.

Animal Model Systems

The invention also provides animal model systems for use in carrying out the screening methods described above. Examples of these

15   model systems include zebrafish and other animals, such as mice, that have mutations in a titin gene. For example, a zebrafish model that can be used in the invention can include a mutation that results in a lack of titin production or production of a truncated (e.g., by introduction of a stop codon) or otherwise altered titin gene product. The mutation can, for

20   example, result in the presence of a stop codon in a cardiac-specific exon, such as the N2B exon (e.g., in the IS3 region; see below). The mutation can be in a region encoding the I band, resulting in the production of a protein in which the I band is truncated and the A band and M line are absent, or can be in a region encoding another portion of the molecule,

25   such as the A band or M line region. As a specific example, a zebrafish having the pickwick mutation can be used.

20

Experimental Results

During a large-scale mutagenesis screening of the zebrafish
genome, a group of mutations were identified that affect cardiac
contractility. One of these mutations, called *pickwick* (*pik*), dramatically
5   reduces the function of both chambers, causing a recessive, lethal form of
heart failure in the zebrafish embryo.

Direct *in vivo* recording of ventricular pressures by the null balance
feedback system shows that *pickwick* causes a 5.8 fold reduction of peak
systolic pressures, compared to age-matched controls (0.084+/- 0.008 vs.
10   0.49+/- 0.06 mm Hg). Morphological analysis of *pickwick* revealed a
stretched and thin myocardium, excess cardiac jelly, absent A-V cushions,
and an obstructed ventricular outflow tract. Extensive ultrastructural
defects were found by transmission electron microscopy, affecting the
assembly of Z-discs and the organization of myofilaments. Reciprocal
15   blastomere transplants identified *pickwick* as a cell autonomously acting
mutation of the myoblast lineage.

A positional cloning approach was adopted for gene identification.
The *pickwick* mutation has been assigned to a small chromosomal interval,
which is covered by BAC clones. The *titin* gene spans this interval, and
20   thus the *pickwick* phenotype is due to a mutation in the *titin* gene. In
particular, the *pickwick* gene was mapped to linkage group (LG) 9 by bulk
segregant analysis using the *pikm242* allele, which is one of five cardiac
specific alleles (*pikm242, pikm171, pikm740, pikm186, pikmnm2*). A
panel of Z-markers in the linkage group was tested for simple sequence
25   length polymorphisms (SSLPs) using 931 homozygous mutant embryos.
Markers Z8363 and Z26463 were shown to flank the *pickwick* locus,
defining a 1.2 cM interval containing the gene. It is estimated that 1 cM
corresponds to 500-600 kb DNA in the zebrafish genome (Postlethwait *et*

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al., *Science* 264:699-703, 1994). We thus initiated chromosomal walking from the Z8363 marker, which is 0.7 cM from the mutation (12 recombinants out of 1750 meioses).

A positive YAC clone (YAC5) was identified that had a T7 end that
5   is highly homologous to human *titin* coding sequences. As the *titin*
genomic region was estimated to be over 300 kb in humans, we decided to
identify BAC clones based on sequence information of the zebrafish *titin*
EST clones. A physical contig was constructed based on these sequences,
which covers the whole *titin* genomic area. Single stranded
10   conformational polymorphisms (SSCPs) were developed from the ends
and internal sequences of these clones were used for fine recombinational
mapping. One SSCP marker inside the *titin* genomic area (B9F2) picked
up one recombinant from the Z26463 side. The other four SSCP markers
inside the *titin* genomic area (B4SP1, B2T7, B7SP, and B6SP) picked up
15   zero recombinants out of 1750 meioses. These genetic data indicated that
the *pickwick* locus is very close to or within the *titin* genomic region.

As the *titin* cDNA alone is around 82 kb, rescuing the phenotype by
RNA injection could prove to be quite difficult. However, we found
evidence that the *pickwick* locus is within the *titin* gene by identification of
20   point mutations in one of the *pickwick* alleles. As most of the alleles of
pickwick have a cardiac-specific phenotype, we presumed that the point
mutation is located in a cardiac-specific exon. We focused on the N2B
domain in the I-band of titin, as all of the cardiac isoforms are N2B
domain based. The zebrafish N2B domain was cloned by RT-PCR. It is a
25   4.3 kb cDNA encoding infrastructures similar to those in humans and
mice, and contains 4 IG repeats and three unique sequences, including
longer IS3 and shorter IS1.

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N2B domains from *pickwick* mutant embryos were then cloned.
RNA mismatch analysis was performed to identify the location of the
point mutation. One mismatch between the PCR products from *pikm171*
and *pikm242* was identified. Sequencing of the PCR product resulted in

5   the identification of a T-> G transition in the *pikm171* allele. This
mutation resulted in a change of leucine in the IS3 fragment of N2B
domain (N2B-IS3) into a stop codon. The mutation was confirmed in all
of the seven homozygous *pikm171* mutant embryos, but none of the four
pikm242 homozygous embryos. A truncated version of titin is predicted to

10 be in the *pikm171* mutant, only as a cardiac specific isoform. It should
contain the Z-disc and part of the I-band and be sized around 4,000 amino
acids, based on comparison to the homologous human titin sequence,
which has a full length of 27,000 amino acids. The identification of a non-
sense mutation in the cardiac specific N2B domain in *pikm171* allele

15 confirmed the hypothesis that *titin* is the *pickwick* gene.

Titin was expressed in the zebrafish embryo during the period when
the *pickwick* phenotype was first detected. Whole mount *in situ*
hybridization analysis indicated that *titin* was expressed strongly in both
the heart and the somites at 24 hpf. *Titin* mRNA expression in the heart is

20 normal in *pikm171*. We confirmed the notion that N2B is a cardiac-
specific exon in zebrafish by labeling a probe in the IS3 domain for the
whole mount *in situ* hybridization.

The identification of a point mutation in the N2B domain thus
establishes *pickwick* as the first *in vivo* vertebrate system to study the

25 functions of titin in the heart. If titin functions as a spring, as proposed, it
is expected that the contraction will be much weaker. This is exactly what
we observed in pickwick mutant embryos. If titin functions as a template
during the sarcomere assembly, a "silent heart" phenotype would be

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expected in titin null mutation. According to the current model of the

myofibrillogenesis (Dabiri *et al.*, Proc. Natl. Acad. Sci. U.S.A. 94:9493-

9498, 1997), the thick element and/or the sarcomere could not assemble

into a beating machine. In contrast, the hearts in the homozygous *pikm171*

5   mutant embryos and all of the other *pickwick* alleles still beat, despite

being weaker.

The mutation in *pikm171* predicts a truncated protein in which most

of the elastic I-band is deleted and the C-terminal A-band and M-line

regions eliminated. It thus could be considered as a null mutation in terms

10   of function as a spring and a potential dominant negative mutation in terms

of its function as a template for sarcomere assembly (Turnacioglu *et al.*,

Mol. Biol. Cell 8:705-717, 1997). The observation of the weak beating in

the *pickwick* mutant embryos suggested the existence of primary

contractile machinery without titin. Indeed, thick and thin elements can be

15   detected in the ventricular myocardium cells. They have the capacity to

assemble into a functional beating structure in the absence of titin.

We thus have carried out a detailed physiological and

morphological analysis of *pickwick*, a zebrafish heart function mutation

that reduces the contractility of both chambers. Several pieces of evidence

20   pointed out that *titin* is the *pickwick* gene. Genetic analysis linked the

pickwick locus closely to the *titin* genomic area. The identification of the

pikmVO62H, a *pickwick* allele that has an additional somite phenotype,

can be explained by the titin hypothesis. The point mutation is expected to

be in the common exons that are shared between the cardiac and somatic

25   isoforms of titin. Evidence confirming this hypothesis came from the

identification of a point mutation in the cardiac specific N2B domain of

titin in one of the *pickwick* alleles, *pikm171*. We went on to show that

sarcomere structure is disrupted in the myocardium cells of *pikm171*, but

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not the somatic muscle cells. The expression pattern of titin is consistent with this phenotype. Strong expression in both cardiac and skeletal muscles was detected at the onset of the *pickwick* phenotype.

Thus, our observation in zebrafish is in consistent with the notion
5 that titin functions as a spring during the muscle contraction. As titin is a sarcomere structure protein, it is conceivable that myocardium is affected cell-autonomously in *pickwick* mutant embryos. The thin and stretched morphology could be due to the mechanic tension generated from the failure to form higher-order sarcomere structure and the loss of spring.
10 The mechanic tension may also be the reason for the separation between the myocardium cells and endocardium cells, generating the excess cardiac jelly. However, there is a possibility that the differentiation program of the myocardium was affected in the *titin* mutation. The valve formation phenotype in *pickwick* mutant embryos could be a secondary defect. It has
15 been suggested that the process of endothelial invasion during valve formation is under control of a localized myocardial signal. (For a review, see Fishman *et al.*, Development 124:2099-2117, 1997.) The physical distance between myocardium and endocardium and/or the stalked differential program in the myocardium could be the reason that prevents a
20 normal cushion formation.

Material and Methods

Zebrafish strains and maintenance

Zebrafish were maintained and staged as described. *pikm242*, *pikm171*, *pikm740*, *pikm186* were generated in a screen on the AB
25 background (Stainier *et al.*, Development 123:285-292, 1996). *pikmVO62H* and *pikmnml2* were generated in a screen on the TL background. Mapping strains were constructed by crossing *pikm242* into

25

india strain. *pikm171* embryos used in expression analysis and EM were
obtained from pair wise matings of *pikm171*/TL heterozygotes.

In situ hybridization

Whole mount *in situ* hybridization was performed as described
5   (Thisse *et·al.*, Development 119:1203-1215, 1993). T5 probe was
generated by digestion of the EST clone AI629069 (Research Genetics).
The N2B and N2A probe were generated through PCR with a tagged T7
promoter. The primer pairs are:

P238F: 5'-AGGGACACTCAGAGACCATAG (SEQ ID NO:3); and
10   P3785RT: 5'-
TAATACGACTCACTATAGGGGTCTGAGGATACTCGCCTTC (SEQ
ID NO:4).

Mapping of *pickwick*

Linkage was established using DNA from 16 homozygous
15   mutations and 16 heterozygous or wild type pick *pikm242*/indian embryos
in bulk segregation analysis (Michelmore *et al.*, Proc. Natl. Acad. Sci.
U.S.A. 88:9828-9832, 1991). Z-markers (simple sequence length
polymorphisms, SSLP) were developed in this lab (Knapik *et al.*, Nat.
Genet. 18:338-343, 1998; Shimoda *et al.*, Genomics 58:219-232, 1999).
20   Genotyping products were resolved in 6% PAGE gels.

Chromosomal walking

YAC and BAC clones were screened by PCR as pools of clones
(Research Genetics) according to the manufacturer's instruction. YAC
ends were cloned by plasmid rescue (Zhong *et al.*, Genomics 48:136-138,
25   1998). Chimeric ends were determined by the RH panel (Geisler *et al.*,

Nat. Genet. 23:86-89, 1999). BAC DNA was extracted using the QIAgene

kit and the end sequences were determined by direct sequencing. BLAST-

X was performed to search for homologous sequence in Genebank. EST

clones were generated by Washington University zebrafish EST project

5   and obtained from Research Genetics. Oligonucleotides derived from the

end sequences of YAC and BAC clones were used in standard PCR

reactions to determine clone overlap. Primer pair B9F2 was derived from

a fragment that was generated by digesting BAC5 with BamHI and then

subcloning into the pUC19 vector. This clone can be hit by a primer pair

10   derived form the T7 end of BAC7. Single-strand conformation

polymorphisms (SSCP) were tested on 6% MDE acrylamide (FMC

Bioproducts) gels at 40°C.

Cloning of the zebrafish N2B domain

Long RT-PCR was performed to amplify the N2B domain from

15   adult zebrafish heart mRNA extracts. mRNA was extracted from pools of

ten zebrafish adult hearts using TRIzole reagent (GibcolBRL), as

described. The cDNA was synthesized using SuperScripTMII RNase H-

Reverse Transcriptase (GibcoBRL) and then treated with RNase H. The

primer is derived from EST3: I19R1:

20   5'- TTTGAACCACTTGAAGGTCACACCAGG (SEQ ID NO:5).

Long-PCR was performed using Expand 20kbPlus PCR System (Roch) as

described. The primer pairs are:

I14F1: 5'- GCTAAGAATGACTATGGAGTTGCCACAAGC (SEQ ID

NO:6)

25   I19R2: 5'- TGAACCACTTGAAGGTCACACCAGGAG (SEQ ID NO:7)

The 4.6 kb product was subcloned using TOPO TA Cloning Kit (Invitrogen) as described. The sequence was determined by primer walking. Forty eight reads were aligned by Phred/Phrad software to get a large contig that contains only one reading frame with around three fold

5   coverage.

To amplify the N2B region from the homozygous mutant zebrafish embryos, three overlapping primer pairs were designed according to the adult N2B sequence. The contamination from the skeletal muscle specific titin isoform was thus eliminated. mRNA was extracted from pools of ten

10   zebrafish day 2 embryos using TRIzole reagent (GibcoBRL) as described. Sequencing results indicated that the embryonic heart titin contain one less IG domain in the area.

Identification of the point mutation

N2B domains from the homozygous mutant embryos were further

15   amplified by primer pairs that generate six overlapping PCR products sized between 0.6 kb and about 1 kb. RNA mismatch analysis was performed using MutationScreenerTM (Ambion) according to the manufacture's protocol. A mismatch was identified between *pikm171* and *pikm242* using the primer pairs:

20   P238FT:

5'-TAATACGACTCACTATAGGGAGGGACACTCAGAGACCATAG

(SEQ ID NO:8)

P3785RT: 5'-

TAATACGACTCACTATAGGGGTCTGAGGATACTCGCCTTC (SEQ

25   ID NO:9). Sequencing results indicate a T->G non-sense mutation in the cDNA from homozygous *pikm171* embryos.

Genomic sequence in this region was amplified using the primer pair:

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P238F: 5'-AGGGACACTCAGAGACCATAG (SEQ ID NO:10)

P341R: 5'- GGCAATGTTACTCTCTGTTGAG (SEQ ID NO:11)

and sent out directly for sequencing after purification using the Geneclean

Spin Kit (BIO101).

5 Electron Microscopy

Forty eight hour embryos were fixed overnight at 4°C in 1.5%

glutaraldehyde, 1% paraformaldehyde, 70 mM NaPO$_4$ pH 7.2, 3%

Sucrose. They were then washed 3 times for 5 minutes each in 0.1M

cacodylate buffer, pH 7.4.

10 Other Embodiments

Although the present invention has been described with reference to

preferred embodiments, one skilled in the art can easily ascertain its

essential characteristics and without departing from the spirit and scope

thereof, can make various changes and modifications of the invention to

15 adapt it to various usages and conditions. Those skilled in the art will

recognize or be able to ascertain using no more than routine

experimentation, many equivalents to the specific embodiments of the

invention described herein. Such equivalents are intended to be

encompassed in the scope of the present invention.

20 All publications and patents mentioned in this specification are

hereby incorporated by reference.

What is claimed is:

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Claims

1. A method of determining whether a test subject has, or is at risk
of developing, a titin-related disease or condition, said method comprising
analyzing a nucleic acid molecule of a sample from the test subject to
5   determine whether the test subject has a mutation in a *titin* gene, wherein
the presence of said mutation is an indication that said test subject has, or
is at risk of developing, a titin-related disease.

2. The method of claim 1, further comprising the step of using
nucleic acid molecule primers specific for the *titin* gene for nucleic acid
10   molecule amplification of the *titin* gene by the polymerase chain reaction.

3. The method of claim 1, further comprising the step of
sequencing *titin* nucleic acid molecules from said test subject.

4. The method of claim 1, wherein said test subject is a mammal.

5. The method of claim 1, wherein said test subject is human.

15   6. The method of claim 1, wherein said disease or condition is
heart failure.

7. The method of claim 1, wherein said mutation is the *pickwick*
mutation.

8. A method for identifying a compound that can be used to treat or to prevent heart failure, said method comprising contacting an organism comprising a *titin* mutation and having a phenotype characteristic of heart failure with said compound, and determining the effect of said compound 5   on said phenotype, wherein detection of an improvement in said phenotype indicates the identification of a compound that can be used to treat or to prevent heart failure.

9. The method of claim 8, wherein said organism is a zebrafish.

10. The method of claim 8, wherein said *titin* mutation is the 10   *pickwick* mutation.

11. A method of treating or preventing heart failure in a patient, said method comprising administering to said patient a compound identified using the method of claim 8.

12. The method of claim 11, wherein said patient has a mutation in 15   the *titin* gene.

13. The method of claim 12, wherein said mutation is the *pickwick* mutation.

14. A non-human animal comprising a mutation in a *titin* gene.

15. The non-human animal of claim 14, wherein the non-human 20   animal is a zebrafish.

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16. The non-human animal of claim 14, wherein the mutation is in a cardiac-specific exon of said *titin* gene.

17. The non-human animal of claim 16, wherein the mutation is in the N2B exon of said *titin* gene.

5   18. The non-human animal of claim 14, wherein the mutation results in the presence of a stop codon in said *titin* gene.

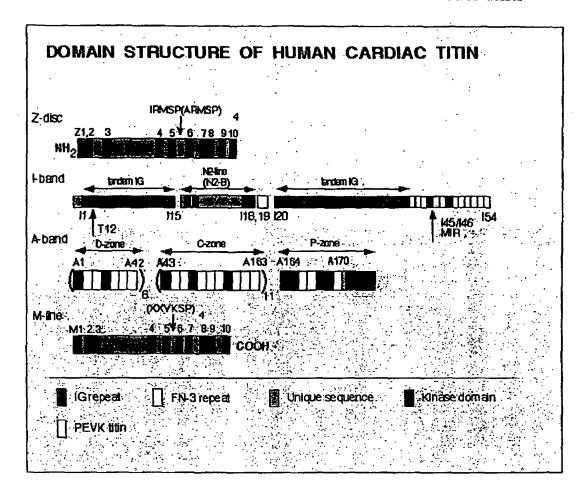19. The non-human animal of claim 14, wherein the mutation is the *pickwick* mutation.

Fig. 1 Domain structure of the titin filament.

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Pro Val Pro Glu Val Ser Trp Phe Arg Asp Gly Gln Val Ile Ser Thr
        35                  40                  45
Ser Thr Leu Pro Gly Val Gln Ile Ser Phe Ser Asp Gly Arg Ala Lys
    50                  55                  60
Leu Thr Ile Pro Ala Val Thr Lys Ala Asn Ser Gly Arg Tyr Ser Leu
65                  70                  75                  80
Lys Ala Thr Asn Gly Ser Gly Gln Ala Thr Ser Thr Ala Glu Leu Leu
                85                  90                  95
Val Lys Ala Glu Thr Ala Pro Pro Asn Phe Val Gln Arg Leu Gln Ser
            100                 105                 110
Met Thr Val Arg Gln Gly Ser Gln Val Arg Leu Gln Val Arg Val Thr
        115                 120                 125
Gly Ile Pro Thr Pro Val Val Lys Phe Tyr Arg Asp Gly Ala Glu Ile
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Gln Ser Ser Leu Asp Phe Gln Ile Ser Gln Glu Gly Asp Leu Tyr Ser
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Leu Leu Ile Ala Glu Ala Tyr Pro Glu Asp Ser Gly Thr Tyr Ser Val
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Asn Ala Thr Asn Ser Val Gly Arg Ala Thr Ser Thr Ala Glu Leu Leu
            180                 185                 190
Val Gln Gly Glu Glu Glu Val Pro Ala Lys Lys Thr Lys Thr Ile Val
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Ser Thr Ala Gln Ile Ser Glu Ser Arg Gln Thr Arg Ile Glu Lys Lys
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Ile Pro Pro Lys Pro Lys Ser Arg Ser Pro Thr Pro Pro Ser Ile Ala
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Ala Lys Ala Gln Leu Ala Arg Gln Gln Ser Pro Ser Pro Ile Arg His
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Ser Pro Ser Pro Val Arg His Val Arg Ala Pro Thr Pro Ser Pro Val
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Arg Ser Val Ser Pro Ala Ala Arg Ile Ser Thr Ser Pro Ile Arg Ser
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Val Arg Ser Pro Leu Leu Met Arg Lys Thr Gln Ala Ser Thr Val Ala
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Thr Gly Pro Glu Val Pro Pro Pro Trp Lys Gln Glu Gly Tyr Val Ala
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Ser Ser Ser Glu Ala Glu Met Arg Glu Thr Thr Leu Thr Thr Ser Thr
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Gln Ile Arg Thr Glu Glu Arg Trp Glu Gly Arg Tyr Gly Val Gln Glu
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Gln Val Thr Ile Ser Gly Ala Ala Gly Ala Ala Ala Ser Val Ser Ala
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Ser Ala Ser Tyr Ala Ala Glu Ala Val Ala Thr Gly Ala Lys Glu Val
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Lys Gln Asp Ala Asp Lys Ser Ala Ala Val Ala Thr Val Val Ala Ala
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Thr Ala Gln Arg Thr Thr Thr Ala Val His Ile Gln Pro Ala Gln
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Glu Gln Val Arg Lys Glu Ala Glu Lys Thr Ala Val Thr Lys Val Val
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Glu Ile Ile Thr Thr Lys Gln Glu Gln Met His Val Thr His Glu Gln
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Ile Arg Lys Glu Thr Glu Lys Thr Phe Val Pro Lys Val Val Ile Ser
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Ala Ala Lys Ala Lys Glu Gln Glu Thr Arg Ile Ser Glu Glu Ile Thr
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Lys Lys Gln Lys Gln Val Thr Gln Glu Ala Ile Met Lys Glu Thr Arg
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Gln Asp Leu Val Ser Arg Gly Arg Glu Gly Ile Thr Thr Lys Arg Glu
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Ala Thr Val Val Ala Ala Val Asp Gln Ala Arg Val Arg Glu Pro Arg
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Glu Pro Gly His Leu Glu Glu Ser Tyr Ala Gln Gln Thr Thr Leu Glu
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Tyr Gly Tyr Lys Glu Arg Ile Ser Ala Ala Lys Val Ala Glu Pro Pro
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Gln Arg Pro Ala Ser Glu Pro His Val Val Pro Lys Ala Val Lys Pro
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Lys Gly Met His Ile Ser Ser Gln Ile Lys Lys Thr Thr Asp Leu Thr
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Thr Glu Arg Leu Val His Val Asp Lys Arg Pro Arg Thr Ala Ser Pro
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His Phe Thr Val Ser Lys Ile Ser Val Pro Lys Thr Glu His Gly Tyr
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Glu Ala Ser Ile Ala Gly Ser Ala Ile Ala Thr Leu Gln Lys Glu Leu
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Ser Ala Thr Ser Ser Ala Gln Lys Ile Thr Lys Ser Val Lys Ala Pro
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Thr Val Lys Pro Ser Glu Thr Arg Val Arg Ala Glu Pro Thr Pro Leu
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Pro Gln Phe Pro Phe Ala Asp Thr Pro Asp Thr Tyr Lys Ser Glu Ala
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Thr Glu Thr Ala Arg Val Pro Ala Pro Val Glu Ile Pro Val Thr Pro
                885                 890                 895
Pro Thr Leu Val Ser Gly Leu Lys Asn Val Thr Val Ile Glu Gly Glu
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Ser Val Thr Leu Glu Cys His Ile Ser Gly Tyr Pro Ser Pro Thr Val
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Thr Trp Tyr Arg Glu Asp Tyr Gln Ile Glu Ser Ser Ile Asp Phe Gln
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His Cys Lys Met Ser Gly Tyr Pro Leu Pro Lys Ile Ala Trp Tyr Lys
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Asp Gly Lys Arg Ile Lys His Gly Glu Arg Tyr Gln Met Asp Phe Leu
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Tyr Lys Pro Val Phe Val Leu Lys Pro Val Ser Phe Lys Cys Leu Glu
      1410              1415              1420
Gly Gln Thr Ala Arg Phe Asp Leu Lys Val Val Gly Arg Pro Met Pro
1425              1430              1435              1440
Glu Thr Phe Trp Phe His Asp Gly Gln Gln Ile Val Asn Asp Tyr Thr
              1445              1450              1455
His Lys Val Val Ile Lys Glu Asp Gly Thr Gln Ser Leu Ile Ile Val
          1460              1465              1470
Pro Ala Thr Pro Ser Asp Ser Gly Glu Trp Thr Val Val Ala Gln Asn
      1475              1480              1485
Arg Ala Gly Arg Ser Ser Ile Ser Val Ile Leu Thr Val Glu Ala Val
      1490              1495              1500
Glu His Gln Val Lys Pro Met Phe Val Glu Lys Leu Lys Asn Val Asn
1505              1510              1515              1520
Ile Lys Glu Gly Ser Arg Leu Glu Met Lys Val Arg Ala Thr Gly Asn
          1525              1530              1535
Pro Asn Pro Asp Ile Val Trp Leu Lys Asn Ser Asp Ile Ile Val Pro
          1540              1545              1550
His Lys Tyr Pro Lys Ile Arg Ile Glu Gly Thr Lys Gly Glu Ala Ala
      1555              1560              1565
Leu Lys Ile Asp Ser Thr Val Ser Gln Asp Ser Ala Trp Tyr Thr Ala
      1570              1575              1580
Thr Ala Ile Asn Lys Ala Gly Arg Asp Thr Thr Arg Cys Lys Val Asn
1585              1590              1595              1600
Val Glu Val Glu Phe Ala Glu Pro Glu Pro Glu Arg Lys Leu Ile Ile
              1605              1610              1615
Pro Arg Gly Thr Tyr Arg Ala Lys Glu Ile Ala Ala Pro Glu Leu Glu
          1620              1625              1630
Pro Leu His Leu Arg Tyr Gly Gln Glu Gln Trp Glu Glu Gly Asp Leu
      1635              1640              1645
Tyr Asp Lys Glu Lys Gln Gln Lys Pro Phe Phe Lys Lys Lys Leu Thr
      1650              1655              1660
Ser Leu Arg Leu Lys Arg Phe Gly Pro Ala His Phe Glu Cys Arg Leu
1665              1670              1675              1680
Thr Pro Ile Ser Asp Pro Thr Met Val Val Glu Trp Leu His Asp Gly
              1685              1690              1695
Lys Pro Leu Glu Ala Ala Asn Arg Leu Arg Met Ile Asn Glu Phe Gly
          1700              1705              1710
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Tyr Cys Ser Leu Asp Tyr Gly Val Ala Tyr Ser Arg Asp Ser Gly Ile
        1715              .       1720               1725
Ile Thr Cys Arg Ala Thr Asn Lys Tyr Gly Thr Asp His Thr Ser Ala
    1730              1735             1740 .
Thr Leu Ile Val Lys Asp Glu Lys Ser Leu Val Glu Glu Ser Gln Leu
1745              1750             1755              1760
Pro Glu Gly Arg Lys Gly Leu Gln Arg Ile Glu Glu Leu Glu Arg Met
            1765              1770             1775
Ala His Glu Gly Ala Leu Thr Gly Val Thr Thr Asp Gln Lys Glu Lys
        1780             1785              1790
Gln Lys Pro Asp Ile Val Leu Tyr Pro Glu Pro Val Arg Val Leu Glu
        1795             1800             1805        .
Gly Glu Thr Ala Arg Phe Arg Cys Arg Val Thr Gly Tyr Pro Gln Pro
    1810             1815             1820
Lys Val Asn Trp Tyr Leu Asn Gly Gln Leu Ile Arg Lys Ser Lys Arg
1825             1830             1835              1840
Phe Arg Val Arg Tyr Asp Gly Ile His Tyr Leu Asp Ile Val Asp Cys
            1845             1850             1855
Lys Ser Tyr Asp Thr Gly Glu Val Lys Val Thr Ala Glu Asn Pro Glu
        1860             1865             1870
Gly Val Ile Glu His Lys Val Lys Leu Glu Ile Gln Gln Arg Glu Asp
        1875             1880             1885
Phe Arg Ser Val Leu Arg Arg Ala Pro Glu Pro Arg Pro Glu Phe His
        1890             1895             1900
Val His Glu Pro Gly Lys Leu Gln Phe Glu Val Gln Lys Val Asp Arg
1905             1910             1915             1920
Pro Val Asp Thr Thr Glu Thr Lys Glu Val Val Lys Leu Lys Arg Ala
            1925             1930             1935
Glu Arg Ile Thr His Glu Lys Val Pro Glu Glu Ser Glu Glu Leu Arg
        1940             1945             1950
Ser Lys Phe Lys Arg Arg Thr Glu Glu Gly Tyr Tyr Glu Ala Ile Thr
    1955             1960             1965
Ala Val Glu Leu Lys Ser Arg Lys Lys Asp Glu Ser Tyr Glu Glu Leu
    1970             1975             1980
Leu Arg Lys Thr Lys Asp Glu Leu Leu His Trp Thr Lys Glu Leu Thr
1985             1990             1995             2000
Glu Glu Glu Lys Lys Ala Leu Ala Glu Glu Gly Lys Ile Thr Ile Pro
            2005             2010             2015
Thr Phe Lys Pro Asp Lys Ile Glu Leu Ser Pro Ser Met Glu Ala Pro
            2020             2025             2030
Lys Ile Phe Glu Arg Ile Gln Ser Gln Thr Val Gly Gln Gly Ser Asp
        2035             2040             2045
Ala His Phe Arg Val Arg Val Val Gly Lys Pro Asp Pro Glu Cys Glu
    2050             2055             2060
Trp Tyr Lys Asn Gly Val Lys Ile Glu Arg Ser Asp Arg Ile Tyr Trp
2065             2070             2075             2080
Tyr Trp Pro Glu Asp Asn Val Cys Glu Leu Val Ile Arg Asp Val Thr
            2085             2090             2095
Ala Glu Asp Ser Ala Ser Ile Met Val Lys Ala Ile Asn Ile Ala Gly
            2100             2105             2110
Glu Thr Ser Ser His Ala Phe Leu Leu Val Gln Ala Lys Gln Leu Ile
        2115             2120             2125
Thr Phe Thr Gln Glu Leu Gln Asp Val Val Ala Lys Glu Lys Asp Thr
    2130             2135             2140
Met Ala Thr Phe Glu Cys Glu Thr Ser Glu Pro Phe Val Lys Val Lys
2145             2150             2155             2160
Trp Tyr Lys Asp Gly Met Glu Val His Glu Gly Asp Lys Tyr Arg Met
            2165             2170             2175
His Ser Asp Arg Lys Val His Phe Leu Ser Ile Leu Thr Ile Asp Thr
        2180             2185             2190
Ser Asp Ala Glu Asp Tyr Ser Cys Val Leu Val Glu Asp Glu Asn Val
        2195             2200             2205
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Lys Thr Thr Ala Lys Leu Ile Val Glu Gly Ala Val Val Glu Phe Val
    2210              2215              2220
Lys Glu Leu Gln Asp Ile Glu Val Pro Glu Ser Tyr Ser Gly Glu Leu
2225              2230              2235              2240
Glu Cys Ile Val Ser Pro Glu Asn Ile Glu Gly Lys Trp Tyr His Asn
              2245              2250              2255
Asp Val Glu Leu Lys Ser Asn Gly Lys Tyr Thr Ile Thr Ser Arg Arg
         2260              2265              2270
Gly Arg Gln Asn Leu Thr Val Lys Asp Val Thr Lys Glu Asp Gln Gly
         2275              2280              2285
Glu Tyr Ser Phe Val Ile Asp Gly Lys Lys Thr Thr Cys Lys Leu Lys
    2290              2295              2300
Met Lys Pro Arg Pro Ile Ala Ile Leu Gln Gly Leu Ser Asp Gln Lys
2305              2310              2315              2320
Val Cys Glu Gly Asp Ile Val Gln Leu Glu Val Lys Val Ser Leu Glu
              2325              2330              2335
Ser Val Glu Gly Val Trp Met Lys Asp Gly Gln Glu Val Gln Pro Ser
         2340              2345              2350
Asp Arg Val His Ile Val Ile Asp Lys Gln Ser His Met Leu Leu Ile
         2355              2360              2365
Glu Asp Met Thr Lys Glu Asp Ala Gly Asn Tyr Ser Phe Thr Ile Pro
    2370              2375              2380
Ala Leu Gly Leu Ser Thr Ser Gly Arg Val Ser Val Tyr Ser Val Asp
2385              2390              2395              2400
Val Ile Thr Pro Leu Lys Asp Val Asn Val Ile Glu Gly Thr Lys Ala
              2405              2410              2415
Val Leu Glu Cys Lys Val Ser Val Pro Asp Val Thr Ser Val Lys Trp
         2420              2425              2430
Tyr Leu Asn Asp Glu Gln Ile Lys Pro Asp Asp Arg Val Gln Ala Ile
         2435              2440              2445
Val Lys Gly Thr Lys Gln Arg Leu Val Ile Asn Arg Thr His Ala Ser
    2450              2455              2460
Asp Glu Gly Pro Tyr Lys Leu Ile Val Gly Arg Val Glu Thr Asn Cys
2465              2470              2475              2480
Asn Leu Ser Val Glu Lys Ile Lys Ile Ile Arg Gly Leu Arg Asp Leu
              2485              2490              2495
Thr Cys Thr Glu Thr Gln Asn Val Val Phe Glu Val Glu Leu Ser His
         2500              2505              2510
Ser Gly Ile Asp Val Leu Trp Asn Phe Lys Asp Lys Glu Ile Lys Pro
         2515              2520              2525
Ser Ser Lys Tyr Lys Ile Glu Ala His Gly Lys Ile Tyr Lys Leu Thr
    2530              2535              2540
Val Leu Asn Met Met Lys Asp Asp Glu Gly Lys Tyr Thr Phe Tyr Ala
2545              2550              2555              2560
Gly Glu Asn Met Thr Ser Gly Lys Leu Thr Val Ala Gly Gly Ala Ile
              2565              2570              2575
Ser Lys Pro Leu Thr Asp Gln Thr Val Ala Glu Ser Gln Glu Ala Val
         2580              2585              2590
Phe Glu Cys Glu Val Ala Asn Pro Asp Ser Lys ·Gly Glu Trp Leu Arg
         2595              2600              2605
Asp Gly Lys His Leu Pro Leu Thr Asn Asn Ile Arg Ser Glu Ser Asp
    2610              2615              2620
Gly His Lys Arg Arg Leu Ile Ile Ala Ala Thr Lys Leu Asp Asp Ile
2625              2630              2635              2640
Gly Glu Tyr Thr Tyr Lys Val Ala Thr Ser Lys Thr Ser Ala Lys Leu
              2645              2650              2655
Lys Val Glu Ala Val Lys Ile Lys Lys Thr Leu Lys Asn Leu Thr Val
              2660              2665              2670
Thr Glu Thr Gln Asp Ala Val Phe Thr Val Glu Leu Thr His Pro Asn
    2675              2680              2685
Val Lys Gly Val Gln Trp Ile Lys Asn Gly Val Val Leu Glu Ser Asn
    2690              2695              2700
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Glu Lys Tyr Ala Ile Ser Val Lys Gly Thr Ile Tyr Ser Leu Arg Ile
2705              2710              2715              2720
Lys Asn Cys Ala Ile Val Asp Glu Ser Val Tyr Gly Phe Arg Leu Gly
         2725              2730              2735
Arg Leu Gly Ala Ser Ala Arg Leu His Val Glu Thr Val Lys Ile Ile
         2740              2745              2750
Lys Lys Pro Lys Asp Val Thr Ala Leu Glu Asn Ala Thr Val Ala Phe
         2755              2760              2765
Glu Val Ser Val Ser His Asp Thr Val Pro Val Lys Trp Phe His Lys
    2770              2775              2780
Ser Val Glu Ile Lys Pro Ser Asp Lys His Arg Leu Val Ser Glu Arg
2785              2790              2795              2800
Lys Val His Lys Leu Met Leu Gln Asn Ile Ser Pro Ser Asp Ala Gly
         2805              2810              2815
Glu Tyr Thr Ala Val Val Gly Gln Leu Glu Cys Lys Ala Lys Leu Phe
         2820              2825              2830
Val Glu Thr Leu His Ile Thr Lys Thr Met Lys Asn Ile Glu Val Pro
    2835              2840              2845
Glu Thr Lys Thr Ala Ser Phe Glu Cys Glu Val Ser His Phe Asn Val
    2850              2855              2860
Pro Ser Met Trp Leu Lys Asn Gly Val Glu Ile Glu Met Ser Glu Lys
2865              2870              2875              2880
Phe Lys Ile Val Val Gln Gly Lys Leu His Gln Leu Ile Ile Met Asn
         2885              2890              2895
Thr Ser Thr Glu Asp Ser Ala Glu Tyr Thr Phe Val Cys Gly Asn Asp
         2900              2905              2910
Gln Val Ser Ala Thr Leu Thr Val Thr Pro Ile Met Ile Thr Ser Met
         2915              2920              2925
Leu Lys Asp Ile Asn Ala Glu Glu Lys Asp Thr Ile Thr Phe Glu Val
    2930              2935              2940
Thr Val Asn Tyr Glu Gly Ile Ser Tyr Lys Trp Leu Lys Asn Gly Val
2945              2950              2955              2960
Glu Ile Lys Ser Thr Asp Lys Cys Gln Met Arg Thr Lys Lys Leu Thr
         2965              2970              2975
His Ser Leu Asn Ile Arg Asn Val His Phe Gly Asp Ala Ala Asp Tyr
         2980              2985              2990
Thr Phe Val Ala Gly Lys Ala Thr Ser Thr Ala Thr Leu Tyr Val Glu
         2995              3000              3005
Ala Arg His Ile Glu Phe Arg Lys His Ile Lys Asp Ile Lys Val Leu
    3010              3015              3020
Glu Lys Lys Arg Ala Met Phe Glu Cys Glu Val Ser Glu Pro Asp Ile
3025              3030              3035              3040
Thr Val Gln Trp Met Lys Asp Asp Gln Glu Leu Gln Ile Thr Asp Arg
         3045              3050              3055
Ile Lys Ile Gln Lys Glu Lys Tyr Val His Arg Leu Leu Ile Pro Ser
         3060              3065              3070
Thr Arg Met Ser Asp Ala Gly Lys Tyr Thr Val Val Ala Gly Gly Asn
    3075              3080              3085
Val Ser Thr Ala Lys Leu Phe Val Glu Gly Arg Asp Val Arg Ile Arg
    3090              3095              3100
Ser Ile Lys Lys Glu Val Gln Val Ile Glu Lys Gln Arg Ala Val Val
3105              3110              3115              3120
Glu Phe Glu Val Asn Glu Asp Asp Val Asp Ala His Trp Tyr Lys Asp
         3125              3130              3135
Gly Ile Glu Ile Asn Phe Gln Val Gln Glu Arg His Lys Tyr Val Val
         3140              3145              3150
Glu Arg Arg Ile His Arg Met Phe Ile Ser Glu Thr Arg Gln Ser Asp
    3155              3160              3165
Ala Gly Glu Tyr Thr Phe Val Ala Gly Arg Asn Arg Ser Ser Val Thr
    3170              3175              3180
Leu Tyr Val Asn Ala Pro Glu Pro Pro Gln Val Leu Gln Glu Leu Gln
3185              3190              3195              3200
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Pro Val Thr Val Gln Ser Gly Lys Pro Ala Arg Phe Cys Ala Met Ile
          3205              3210              3215
Ser Gly Arg Pro Gln Pro Lys Ile Ser Trp Tyr Lys Glu Glu Gln Leu
          3220              3225              3230
Leu Ser Thr Gly Phe Lys Cys Lys Phe Leu His Asp Gly Gln Glu Tyr
          3235              3240    ·         3245
Thr Leu Leu Ile Glu Ala Phe Pro Glu Asp Ala Ala Val Tyr Thr
          3250              3255              3260
Cys Glu Ala Lys Asn Asp Tyr Gly Val Ala Thr Thr Ser Ala Ser Leu
3265              3270              3275              3280
Ser Val Glu Val Pro Glu Val Val Ser Pro Asp Gln Glu Met Pro Val
          3285              3290              3295
Tyr Pro Pro Ala Ile Ile Thr Pro Leu Gln Asp Thr Val Thr Ser Glu
          3300              3305              3310
Gly Gln Pro Ala Arg Phe Gln Cys Arg Val Ser Gly Thr Asp Leu Lys .
          3315              3320              3325
Val Ser Trp Tyr Ser Lys Asp Lys Lys Ile Lys Pro Ser Arg Phe Phe
          3330              3335              3340
Arg Met Thr Gln Phe Glu Asp Thr Tyr Gln Leu Glu Ile Ala Glu Ala
3345              3350              3355              3360
Tyr Pro Glu Asp Glu Gly Thr Tyr Thr Phe Val Ala Asn Asn Ala Val
          3365              3370              3375
Gly Gln Val Ser Ser Thr Ala Asn Leu Ser Leu Glu Ala Pro Glu Ser
          3380              3385              3390
Ile Leu His Glu Arg Ile Glu Gln Glu Ile Glu Met Glu Met Lys Glu
          3395              3400.             3405
Phe Ser Ser Ser Phe Leu Ser Ala Glu Glu Glu Gly Leu His Ser Ala
          3410              3415              3420
Glu Leu Gln Leu Ser Lys Ile Asn Glu Thr Leu Glu Leu Leu Ser Glu
3425              3430              3435              3440
Ser Pro Val Tyr Pro Thr Lys Phe Asp Ser Glu Lys Glu Gly Thr Gly
          .3445             3450              3455
Pro Ile Phe Ile Lys Glu Val Ser Asn Ala Asp Ile Ser Met Gly Asp
          3460              3465              3470
Val Ala Thr Leu Ser Val Thr Val Ile Gly Ile Pro Lys Pro Lys Ile
          3475              3480              3485
Gln Trp Phe Phe Asn Gly Val Leu Leu Thr Pro Ser Ala Asp Tyr Lys
          3490              3495              3500
Phe Val Phe Asp Gly Asp Asp His Ser Leu Ile Ile Leu Phe Thr Lys
3505              3510              3515              3520
Leu Glu Asp Glu Gly Glu Tyr Thr Cys Met Ala Ser Asn Asp Tyr Gly
          ·3525             3530              3535
Lys Thr Ile Cys Ser Ala Tyr Leu Lys Ile Asn Ser Lys Gly Glu Gly
          3540              3545              3550
His Lys Asp Thr Glu Thr Glu Ser Ala Val Ala Lys Ser Leu Glu Lys
          3555              3560              3565
Leu Gly Gly Pro Cys Pro Pro His Phe Leu Lys Glu Leu Lys Pro Ile
3570              3575              3580
Arg Cys Ala Gln Gly Leu Pro Ala Ile Phe Glu Tyr Thr Val Val Gly
3585              3590              3595              3600
Glu Pro Ala Pro Thr Val Thr Trp Phe Lys Glu Asn Lys Gln Leu Cys
          3605              3610              3615
Thr Ser Val Tyr Tyr Thr Ile Ile His Asn Pro Asn Gly Ser Gly Thr
          3620              3625              3630
·Phe Ile Val Asn Asp Pro Gln Arg Glu Asp Ser Gly Leu Tyr Ile Cys
          3635              3640              3645
Lys Ala Glu Asn Met Leu Gly Glu Ser Thr Cys Ala Ala Glu Leu Leu
          3650              3655              3660
Val Leu Leu Glu Asp Thr Asp Met Thr Asp Thr Pro Cys Lys Ala Lys
3665              3670              3675              3680
Ser Thr ·Pro Glu Ala Pro Glu Asp Phe Pro Gln Thr Pro Leu Lys Gly
          3685              3690              3695
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Pro Ala Val Glu Ala Leu Asp Ser Glu Gln Glu Ile Ala Thr Phe Val
        3700   3705   3710
Lys Asp Thr Ile Leu Lys Ala Ala Leu Ile Thr Glu Glu Asn Gln Gln
        3715   3720   3725
Leu Ser Tyr Glu His Ile Ala Lys Ala Asn Glu Leu Ser Ser Gln Leu
        3730   3735   3740
Pro Leu Gly Ala Gln Glu Leu Gln Ser Ile Leu Glu Gln Asp Lys Leu
    3745   3750   3755   3760
Thr Pro Glu Ser Thr Arg Glu Phe Leu Cys Ile Asn Gly Ser Ile His
        3765   3770   3775
Phe Gln Pro Leu Lys Glu Pro Ser Pro Asn Leu Gln Leu Gln Ile Val
        3780   3785   3790
Gln Ser Gln Lys Thr Phe Ser Lys Glu Gly Ile Leu Met Pro Glu Glu
        3795   3800   3805
Pro Glu Thr Gln Ala Val Leu Ser Asp Thr Glu Lys Ile Phe Pro Ser
    3810   3815   3820
Ala Met Ser Ile Glu Gln Ile Asn Ser Leu Thr Val Glu Pro Leu Lys
3825   3830   3835   3840
Thr Leu Leu Ala Glu Pro Glu Gly Asn Tyr Pro Gln Ser Ser Ile Glu
            3845   3850   3855
Pro Pro Met His Ser Tyr Leu Thr Ser Val Ala Glu Glu Val Leu Ser
        3860   3865   3870
Leu Lys Glu Lys Thr Val Ser Asp Thr Asn Arg Glu Gln Arg Val Thr
        3875   3880   3885
Leu Gln Lys Gln Glu Ala Gln Ser Ala Leu Ile Leu Ser Gln Ser Leu
    3890   3895   3900
Ala Glu Gly His Val Glu Ser Leu Gln Ser Pro Asp Val Met Ile Ser
3905   3910   3915   3920
Gln Val Asn Tyr Glu Pro Leu Val Pro Ser Glu His Ser Cys Thr Glu
            3925   3930   3935
Gly Gly Lys Ile Leu Ile Glu Ser Ala Asn Pro Leu Glu Asn Ala Gly
            3940   3945   3950
Gln Asp Ser Ala Val Arg Ile Glu Glu Gly Lys Ser Leu Arg Phe Pro
    3955   3960   3965
Leu Ala Leu Glu Glu Lys Gln Val Leu Leu Lys Glu Glu His Ser Asp
    3970   3975   3980
Asn Val Val Met Pro Pro Asp Gln Ile Ile Glu Ser Lys Arg Glu Pro
3985   3990   3995   4000
Val Ala Ile Lys Lys Val Gln Glu Val Gln Gly Arg Asp Leu Leu Ser
            4005   4010   4015
Lys Glu Ser Leu Leu Ser Gly Ile Pro Glu Glu Gln Arg Leu Asn Leu
            4020   4025   4030
Lys Ile Gln Ile Cys Arg Ala Leu Gln Ala Ala Val Ala Ser Glu Gln
        4035   4040   4045
Pro Gly Leu Phe Ser Glu Trp Leu Arg Asn Ile Glu Lys Val Glu Val
    4050   4055   4060
Glu Ala Val Asn Ile Thr Gln Glu Pro Arg His Ile Met Cys Met Tyr
4065   4070   4075   4080
Leu Val Thr Ser Ala Lys Ser Val Thr Glu Glu Val Thr Ile Ile Ile
            4085   4090   4095
Glu Asp Val Asp Pro Gln Met Ala Asn Leu Lys Met Glu Leu Arg Asp
            4100   4105   4110
Ala Leu Cys Ala Ile Ile Tyr Glu Glu Ile Asp Ile Leu Thr Ala Glu
    4115   4120   4125
Gly Pro Arg Ile Gln Gln Gly Ala Lys Thr Ser Leu Gln Glu Glu Met
    4130   4135   4140
Asp Ser Phe Ser Gly Ser Gln Lys Val Glu Pro Ile Thr Glu Pro Glu
4145   4150   4155   4160
Val Glu Ser Lys Tyr Leu Ile Ser Thr Glu Glu Val Ser Tyr Phe Asn
            4165   4170   4175
Val Gln Ser Arg Val Lys Tyr Leu Asp Ala Thr Pro Val Thr Lys Gly
            4180   4185   4190

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Val Ala Ser Ala Val Val Ser Asp Glu Lys Gln Asp Glu Ser Leu Lys
        4195                4200                4205
Pro Ser Glu Glu Lys Glu Glu Ser Ser Ser Glu Ser Gly Thr Glu Glu
    4210                4215                4220
Val Ala Thr Val Lys Ile Gln Glu Ala Glu Gly Gly Leu Ile Lys Glu
4225                4230                4235                4240
Asp Gly Pro Met Ile His Thr Pro Leu Val Asp Thr Val Ser Glu Glu
            4245                4250                4255
Gly Asp Ile Val His Leu Thr Thr Ser Ile Thr Asn Ala Lys Glu Val
        4260                4265                4270
Asn Trp Tyr Phe Glu Asn Lys Leu Val Pro Ser Asp Glu Lys Phe Lys
    4275                4280                4285
Cys Leu Gln Asp Gln Asn Thr Tyr Thr Leu Val Ile Asp Lys Val Asn
    4290                4295                4300
Thr Glu Asp His Gln Gly Glu Tyr Val Cys Glu Ala Leu Asn Asp Ser
4305                4310                4315                4320
Gly Lys Thr Ala Thr Ser Ala Lys Leu Thr Val Val Lys Arg Ala Ala
            4325                4330                4335
Pro Val Ile Lys Arg Lys Ile Glu Pro Leu Glu Val Ala Leu Gly His
        4340                4345                4350
Leu Ala Lys Phe Thr Cys Glu Ile Gln Ser Ala Pro Asn Val Arg Phe
        4355                4360                4365
Gln Trp Phe Lys Ala Gly Arg Glu Ile Tyr Glu Ser Asp Lys Cys Ser
    4370                4375                4380
Ile Arg Ser Ser Lys Tyr Ile Ser Ser Leu Glu Ile Leu Arg Thr Gln
4385                4390                4395                4400
Val Val Asp Cys Gly Glu Tyr Thr Cys Lys Ala Ser Asn Glu Tyr Gly
            4405                4410                4415
Ser Val Ser Cys Thr Ala Thr Leu Thr Val Thr Val Pro Gly Gly Glu
            4420                4425                4430
Lys Lys Val Arg Lys Leu Leu Pro Glu Arg Lys Pro Glu Pro Lys Glu
        4435                4440                4445
Glu Val Val Leu Lys Ser Val Leu Arg Lys Arg Pro Glu Glu Glu Glu
    4450                4455                4460
Pro Lys Val Glu Pro Lys Lys Leu Glu Lys Val Lys Lys Pro Ala Val
4465                4470                4475                4480
Pro Glu Pro Pro Pro Pro Lys Pro Val Glu Glu Val Glu Val Pro Thr
            4485                4490                4495
Val Thr Lys Arg Glu Arg Lys Ile Pro Glu Pro Thr Lys Val Pro Glu
        4500                4505                4510
Ile Lys Pro Ala Ile Pro Leu Pro Ala Pro Glu Pro Lys Pro Lys Pro
    4515                4520                4525
Glu Ala Glu Val Lys Thr Ile Lys Pro Pro Pro Val Glu Pro Glu Pro
    4530                4535                4540
Thr Pro Ile Ala Ala Pro Val Thr Val Pro Val Val Gly Lys Lys Ala
4545                4550                4555                4560
Glu Ala Lys Ala Pro Lys Glu Glu Ala Ala Lys Pro Lys Gly Pro Ile
            4565                4570                4575
Lys Gly Val Pro Lys Lys Thr Pro Ser Pro Ile Glu Ala Glu Arg Arg
        4580                4585                4590
Lys Leu Arg Pro Gly Ser Gly Gly Glu Lys Pro Pro Asp Glu Ala Pro
        4595                4600                4605
Phe Thr Tyr Gln Leu Lys Ala Val Pro Leu Lys Phe Val Lys Glu Ile
    4610                4615                4620
Lys Asp Ile Ile Leu Thr Glu Ser Glu Phe Val Gly Ser Ser Ala Ile
4625                4630                4635                4640
Phe Glu Cys Leu Val Ser Pro Ser Thr Ala Ile Thr Thr Trp Met Lys
            4645                4650                4655
Asp Gly Ser Asn Ile Arg Glu Ser Pro Lys His Arg Phe Ile Ala Asp
            4660                4665                4670
Gly Lys Asp Arg Lys Leu His Ile Ile Asp Val Gln Leu Ser Asp Ala
        4675                4680                4685
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Gly Glu Tyr Thr Cys Val Leu Arg Leu Gly Asn Lys Glu Lys Thr Ser
    4690                4695                4700
Thr Ala Lys Leu Val Val Glu Glu Leu Pro Val Arg Phe Val Lys Thr
4705                4710                4715                4720
Leu Glu Glu Glu Val Thr Val Val Lys Gly Gln Pro Leu Tyr Leu Ser
                4725                4730                4735
Cys Glu Leu Asn Lys Glu Arg Asp Val Val Trp Arg Lys Asp Gly Lys
            4740                4745                4750
Ile Val Val Glu Lys Pro Gly Arg Ile Val Pro Gly Val Ile Gly Leu
            4755                4760                4765
Met Arg Ala Leu Thr Ile Asn Asp Ala Asp Asp Thr Asp Ala Gly Thr
    4770                4775                4780
Tyr Thr Val Thr Val Glu Asn Ala Asn Asn Leu Glu Cys Ser Ser Cys
4785                4790                4795                4800
Val Lys Val Val Glu Val Ile Arg Asp Trp Leu Val Lys Pro Ile Arg
                4805                4810                4815
Asp Gln His Val Lys Pro Lys Gly Thr Ala Ile Phe Ala Cys Asp Ile
            4820                4825                4830
Ala Lys Asp Thr Pro Asn Ile Lys Trp Phe Lys Gly Tyr Asp Glu Ile
        4835                4840                4845
Pro Ala Glu Pro Asn Asp Lys Thr Glu Ile Leu Arg Asp Gly Asn His
    4850                4855                4860
Leu Tyr Leu Lys Ile Lys Asn Ala Met Pro Glu Asp Ile Ala Glu Tyr
4865                4870                4875                4880
Ala Val Glu Ile Glu Gly Lys Arg Tyr Pro Ala Lys Leu Thr Leu Gly
                4885                4890                4895
Glu Arg Glu Val Glu Leu Leu Lys Pro Ile Glu Asp Val Thr Ile Tyr
            4900                4905                4910
Glu Lys Glu Ser Ala Ser Phe Asp Ala Glu Ile Ser Glu Ala Asp Ile
        4915                4920                4925
Pro Gly Gln Trp Lys Leu Lys Gly Glu Leu Leu Arg Pro Ser Pro Thr
    4930                4935                4940
Cys Glu Ile Lys Ala Glu Gly Gly Lys Arg Phe Leu Thr Leu His Lys
4945                4950                4955                4960
Val Lys Leu Asp Gln Ala Gly Glu Val Leu Tyr Gln Ala Leu Asn Ala
                4965                4970                4975
Ile Thr Thr Ala Ile Leu Thr Val Lys Glu Ile Glu Leu Asp Phe Ala
            4980                4985                4990
Val Pro Leu Lys Asp Val Thr Val Pro Glu Arg Arg Gln Ala Arg Phe
    4995                5000                5005
Glu Cys Val Leu Thr Arg Glu Ala Asn Val Ile Trp Ser Lys Gly Pro
    5010                5015                5020
Asp Ile Ile Lys Ser Ser Asp Lys Phe Asp Ile Ile Ala Asp Gly Lys
5025                5030                5035                5040
Lys His Ile Leu Val Ile Asn Asp Ser Gln Phe Asp Asp Glu Gly Val
                5045                5050                5055
Tyr Thr Ala Glu Val Glu Gly Lys Lys Thr Ser Ala Arg Leu Phe Val
            5060                5065                5070
Thr Gly Ile Arg Leu Lys Phe Met Ser Pro Leu Glu Asp Gln Thr Val
        5075                5080                5085
Lys Glu Gly Glu Thr Ala Thr Phe Val Cys Glu Leu Ser His Glu Lys
    5090                5095                5100
Met His Val Val Trp Phe Lys Asn Asp Ala Lys Leu His Thr Ser Arg
5105                5110                5115                5120
Thr Val Leu Ile Ser Ser Glu Gly Lys Thr His Lys Leu Glu Met Lys
                5125                5130                5135
Glu Val Thr Leu Asp Asp Ile Ser Gln Ile Lys Ala Gln Val Lys Glu
            5140                5145                5150
Leu Ser Ser Thr Ala Gln Leu Lys Val Leu Glu Ala Asp Pro Tyr Phe
            5155                5160                5165
Thr Val Lys Leu His Asp Lys Thr Ala Val Glu Lys Asp Glu Ile Thr
    5170                5175                5180
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Leu Lys Cys Glu Val Ser Lys Asp Val Pro Val Lys Trp Phe Lys Asp
5185                5190                5195                5200
Gly Glu Glu Ile Val Pro Ser Pro Lys Tyr Ser Ile Lys Ala Asp Gly
            5205                5210                5215
Leu Arg Arg Ile Leu Lys Ile Lys Lys Ala Asp Leu Lys Asp Lys Gly
            5220                5225                5230
Glu Tyr Val Cys Asp Cys Gly Thr Asp Lys Thr Lys Ala Asn Val Thr
        5235                5240                5245
Val Glu Ala Arg Leu Ile Glu Val Glu Lys Pro Leu Tyr Gly Val Glu
        5250                5255                5260
Val Phe Val Gly Glu Thr Ala His Phe Glu Ile Glu Leu Ser Glu Pro
5265                5270                5275                5280
Asp Val His Gly Gln Trp Lys Leu Lys Gly Gln Pro Leu Thr Ala Ser
            5285                5290                5295
Pro Asp Cys Glu Ile Ile Glu Asp Gly Lys Lys His Ile Leu Ile Leu
            5300                5305                5310
His Asn Cys Gln Leu Gly Met Thr Gly Glu Val Ser Phe Gln Ala Ala
        5315.               5320                5325
Asn Ala Lys Ser Ala Ala Asn Leu Lys Val Lys Glu Leu Pro Leu Ile
        5330                5335                5340
Phe Ile Thr Pro Leu Ser Asp Val Lys Val Phe Glu Lys Asp Glu Ala
5345                5350                5355                5360
Lys Phe Glu Cys Glu Val Ser Arg Glu Pro Lys Thr Phe Arg Trp Leu
            5365                5370                5375
Lys Gly Thr Gln Glu Ile Thr Gly Asp Arg Phe Glu Leu Ile Lys
            5380                5385                5390
Asp Gly Thr Lys His Ser Met Val Ile Lys Ser Ala Ala Phe Glu Asp
            5395                5400                5405
Glu Ala Lys Tyr Met Phe Glu Ala Glu Asp Lys His Thr Ser Gly Lys
        5410                5415                5420
Leu Ile Ile Glu Gly Ile Arg Leu Lys Phe Leu Thr Pro Leu Lys Asp
5425                5430                5435                5440
Val Thr Ala Lys Glu Lys Glu Ser Ala Val Phe Thr Val Glu Leu Ser
            5445                5450                5455
His Asp Asn Ile Arg Val Lys Trp Phe Lys Asn Asp Gln Arg Leu His
            5460                5465                5470
Thr Thr Arg Ser Val Ser Met Gln Asp Glu Gly Lys Thr His Ser Ile
        5475                5480                5485
Thr Phe Lys Asp Leu Ser Ile Asp Asp Thr Ser Gln Ile Arg Val Glu
        5490                5495                5500
Ala Met Gly Met Ser Ser Glu Ala Lys Leu Thr Val Leu Glu Gly Asp
5505                5510                5515                5520
Pro Tyr Phe Thr Gly Lys Leu Gln Asp Tyr Thr Gly Val Glu Lys Asp
            5525                5530                5535
Glu Val Ile Leu Gln Cys Glu Ile Ser Lys Ala Asp Ala Pro Val Lys
            5540                5545                5550
Trp Phe Lys Asp Gly Lys Glu Ile Lys Pro Ser Lys Asn Ala Val Ile
        5555                5560                5565
Lys Thr Asp Gly Lys Lys Arg Met Leu Ile Leu Lys Lys Ala Leu Lys
        5570                5575                5580
Ser Asp Ile Gly Gln Tyr Thr Cys Asp Cys Gly Thr Asp Lys Thr Ser
5585                5590                5595                5600
Gly Lys Leu Asp Ile Glu Asp Arg Glu Ile Lys Leu Val Arg Pro Leu
            5605                5610                5615
His Ser Val Glu Val Met Glu Thr Glu Thr Ala Arg Phe Glu Thr Glu
            5620                5625                5630
Ile Ser Glu Asp Asp Ile His Ala Asn Trp Lys Leu Lys Gly Glu Ala
        5635                5640                5645
Leu Leu Gln Thr Pro Asp Cys Glu Ile Lys Glu Glu Gly Lys Ile His
        5650                5655                5660
Ser Leu Val Leu His Asn Cys Arg Leu Asp Gln Thr Gly Gly Val Asp
5665                5670                5675                5680
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Phe Gln Ala Ala Asn Val Lys Ser Ser Ala His Leu Arg Val Lys Pro
        5685                    5690                    5695
Arg Val Ile Gly Leu Leu Arg Pro Leu Lys Asp Val Thr Val Thr Ala
        5700                    5705                    5710
Gly Glu Thr Ala Thr Phe Asp Cys Glu Leu Ser Tyr Glu Asp Ile Pro
        5715                5720                    5725
Val Glu Trp Tyr Leu Lys Gly Lys Lys Leu Glu Pro Ser Asp Lys Val
        5730                5735                    5740
Val Pro Arg Ser Glu Gly Lys Val His Thr Leu Thr Leu Arg Asp Val
5745                    5750                    5755                    5760
Lys Leu Glu Asp Ala Gly Glu Val Gln Leu Thr Ala Lys Asp Phe Lys
                5765                    5770                    5775
Thr His Ala Asn Leu Phe Val Lys Glu Pro Pro Val Glu Phe Thr Lys
            5780                    5785                    5790
Pro Leu Glu Asp Gln Thr Val Glu Glu Gly Ala Thr Ala Val Leu Glu
        5795                    5800                    5805
Cys Glu Val Ser Arg Glu Asn Ala Lys Val Lys Trp Phe Lys Asn Gly
        5810                    5815                    5820
Thr Glu Ile Leu Lys Ser Lys Lys Tyr Glu Ile Val Ala Asp Gly Arg
5825                    5830                    5835                    5840
Val Arg Lys Leu Val Ile His Asp Cys Thr Pro Glu Asp Ile Lys Thr
            5845                    5850                    5855
Tyr Thr Cys Asp Ala Lys Asp Phe Lys Thr Ser Cys Asn Leu Asn Val
            5860                    5865                    5870
Val Pro Pro His Val Glu Phe Leu Arg Pro Leu Thr Asp Leu Gln Val
        5875                    5880                    5885
Arg Glu Lys Glu Met Ala Arg Phe Glu Cys Glu Leu Ser Arg Glu Asn
        5890                    5895                    5900
Ala Lys Val Lys Trp Phe Lys Asp Gly Ala Glu Ile Lys Lys Gly Lys
5905                    5910                    5915                    5920
Lys Tyr Asp Ile Ile Ser Lys Gly Ala Val Arg Ile Leu Val Ile Asn
            5925                    5930                    5935
Lys Cys Leu Leu Asp Asp Glu Ala Glu Tyr Ser Cys Glu Val Arg Thr
        5940                    5945                    5950
Ala Arg Thr Ser Gly Met Leu Thr Val Leu Glu Glu Glu Ala Val Phe
        5955                    5960                    5965
Thr Lys Asn Leu Ala Asn Ile Glu Val Ser Glu Thr Asp Thr Ile Lys
        5970                    5975                    5980
Leu Val Cys Glu Val Ser Lys Pro Gly Ala Glu Val Ile Trp Tyr Lys
5985                    5990                    5995                    6000
Gly Asp Glu Glu Ile Ile Glu Thr Gly Arg Tyr Glu Ile Leu Thr Glu
            6005                    6010                    6015
Gly Arg Lys Arg Ile Leu Val Ile Gln Asn Ala His Leu Glu Asp Ala
        6020                    6025                    6030
Gly Asn Tyr Asn Cys Arg Leu Pro Ser Ser Arg Thr Asp Gly Lys Val
        6035                    6040                    6045
Lys Val His Glu Leu Ala Ala Glu Phe Ile Ser Lys Pro Gln Asn Leu
        6050                    6055                    6060
Glu Ile Leu Glu Gly Glu Lys Ala Glu Phe Val Cys Ser Ile Ser Lys
6065                    6070                    6075                    6080
Glu Ser Phe Pro Val Gln Trp Lys Arg Asp Asp Lys Thr Leu Glu Ser
            6085                    6090                    6095
Gly Asp Lys Tyr Asp Val Ile Ala Asp Gly Lys Lys Arg Val Leu Val
        6100                    6105                    6110
Val Lys Asp Ala Thr Leu Gln Asp Met Gly Thr Tyr Val Val Met Val
        6115                    6120                    6125
Gly Ala Ala Arg Ala Ala Ala His Leu Thr Val Ile Glu Lys Leu Arg
        6130                    6135                    6140
Ile Val Val Pro Leu Lys Asp Thr Arg Val Lys Glu Gln Gln Glu Val
6145                    6150                    6155                    6160
Val Phe Asn Cys Glu Val Asn Thr Glu Gly Ala Lys Ala Lys Trp Phe
            6165                    6170                    6175
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Arg Asn Glu Glu Ala Ile Phe Asp Ser Ser Lys Tyr Ile Ile Leu Gln
        6180                    6185                    6190
Lys Asp Leu Val Tyr Thr Leu Arg Ile Arg Asp Ala His Leu Asp Asp
        6195                    6200                    6205
Gln Ala Asn Tyr Asn Val Ser Leu Thr Asn His Arg Gly Glu Asn Val
        6210                    6215                    6220
Lys Ser Ala Ala Asn Leu Ile Val Glu Glu Glu Asp Leu Arg Ile Val
6225                    6230                    6235                    6240
Glu Pro Leu Lys Asp Ile Glu Thr Met Glu Lys Lys Ser Val Thr Phe
                6245                    6250                    6255
Trp Cys Lys Val Asn Arg Leu Asn Val Thr Leu Lys Trp Thr Lys Asn
        6260                    6265                    6270
Gly Glu Glu Val Pro Phe Asp Asn Arg Val Ser Tyr Arg Val Asp Lys
        6275                    6280                    6285
Tyr Lys His Met Leu Thr Ile Lys Asp Cys Gly Phe Pro Asp Glu Gly
        6290                    6295                    6300
Glu Tyr Ile Val Thr Ala Gly Gln Asp Lys Ser Val Ala Glu Leu Leu
6305                    6310                    6315                    6320
Ile Ile Glu Ala Pro Thr Glu Phe Val Glu His Leu Glu Asp Gln Thr
                6325                    6330                    6335
Val Thr Glu Phe Asp Asp Ala Val Phe Ser Cys Gln Leu Ser Arg Glu
        6340                    6345                    6350
Lys Ala Asn Val Lys Trp Tyr Arg Asn Gly Arg Glu Ile Lys Glu Gly
        6355                    6360                    6365
Lys Lys Tyr Lys Phe Glu Lys Asp Gly Ser Ile His Arg Leu Ile Ile
        6370                    6375                    6380
Lys Asp Cys Arg Leu Asp Asp Glu Cys Glu Tyr Ala Cys Gly Val Glu
6385                    6390                    6395                    6400
Asp Arg Lys Ser Arg Ala Arg Leu Phe Val Glu Glu Ile Pro Val Glu
                6405                    6410                    6415
Ile Ile Arg Pro Pro Gln Asp Ile Leu Glu Ala Pro Gly Ala Asp Val
                6420                    6425                    6430
Val Phe Leu Ala Glu Leu Asn Lys Asp Lys Val Glu Val Gln Trp Leu
        6435                    6440                    6445
Arg Asn Asn Met Val Val Val Gln Gly Asp Lys His Gln Met Met Ser
        6450                    6455                    6460
Glu Gly Lys Ile His Arg Leu Gln Ile Cys Asp Ile Lys Pro Arg Asp
6465                    6470                    6475                    6480
Gln Gly Glu Tyr Arg Phe Ile Ala Lys Asp Lys Glu Ala Arg Ala Lys
                6485                    6490                    6495
Leu Glu Leu Ala Ala Ala Pro Lys Ile Lys Thr Ala Asp Gln Asp Leu
                6500                    6505                    6510
Val Val Asp Val Gly Lys Pro Leu Thr Met Val Val Pro Tyr Asp Ala
        6515                    6520                    6525
Tyr Pro Lys Ala Glu Ala Glu Trp Phe Lys Glu Asn Glu Pro Leu Ser
6530                    6535                    6540
Thr Lys Thr Ile Asp Thr Thr Ala Glu Gln Thr Ser Phe Arg Ile Leu
6545                    6550                    6555                    6560
Glu Ala Lys Lys Gly Asp Lys Gly Arg Tyr Lys Ile Val Leu Gln Asn
                6565                    6570                    6575
Lys His Gly Lys Ala Glu Gly Phe Ile Asn Leu Lys Val Ile Asp Val
                6580                    6585                    6590
Pro Gly Pro Val Arg Asn Leu Glu Val Thr Glu Thr Phe Asp Gly Glu
        6595                    6600                    6605
Val Ser Leu Ala Trp Glu Glu Pro Leu Thr Asp Gly Gly Ser Lys Ile
        6610                    6615                    6620
Ile Gly Tyr Val Val Glu Arg Arg Asp Ile Lys Arg Lys Thr Trp Val
6625                    6630                    6635                    6640
Leu Ala Thr Asp Arg Ala Glu Ser Cys Glu Phe Thr Val Thr Gly Leu
                6645                    6650                    6655
Gln Lys Gly Gly Val Glu Tyr Leu Phe Arg Val Ser Ala Arg Asn Arg
                6660                    6665                    6670
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Val Gly Thr Gly Glu Pro Val Glu Thr Asp Asn Pro Val Glu Ala Arg
        6675              6680                6685
Ser Lys Tyr Asp Val Pro Gly Pro Pro Leu Asn Val Thr Ile Thr Asp
    6690              6695                6700
Val Asn Arg Phe Gly Val Ser Leu Thr Trp Glu Pro Pro Glu Tyr Asp
6705              6710              6715              6720
Gly Gly Ala Glu Ile Thr Asn Tyr Val Ile Glu Leu Arg Asp Lys Thr
              6725              6730              6735
Ser Ile Arg Trp Asp Thr Ala Met Thr Val Arg Ala Glu Asp Leu Ser
        6740              6745              6750
Ala Thr Val Thr Asp Val Val Glu Gly Gln Glu Tyr Ser Phe Arg Val
        6755              6760              6765
Arg Ala Gln Asn Arg Ile Gly Val Gly Lys Pro Ser Ala Ala Thr Pro
    6770              6775              6780
Phe Val Lys Val Ala Asp Pro Ile Glu Arg Pro Ser Pro Pro Val Asn
6785              6790              6795              6800
Leu Thr Ser Ser Asp Gln Thr Gln Ser Ser Val Gln Leu Lys Trp Glu
              6805              6810              6815
Pro Pro Leu Lys Asp Gly Gly Ser Pro Ile Leu Gly Tyr Ile Ile Glu
              6820              6825              6830
Arg Cys Glu Glu Gly Lys Asp Asn Trp Ile Arg Cys Asn Met Lys Leu
        6835              6840              6845
Val Pro Glu Leu Thr Tyr Lys Val Thr Gly Leu Glu Lys Gly Asn Lys
    6850              6855              6860
Tyr Leu Tyr Arg Val Ser Ala Glu Asn Lys Ala Gly Val Ser Asp Pro
6865              6870              6875              6880
Ser Glu Ile Leu Gly Pro Leu Thr Ala Asp Asp Ala Phe Val Glu Pro
              6885              6890              6895
Thr Met Asp Leu Ser Ala Phe Lys Asp Gly Leu Glu Val Ile Val Pro
              6900              6905              6910
Asn Pro Ile Thr Ile Leu Val Pro Ser Thr Gly Tyr Pro Arg Pro Thr
        6915              6920              6925
Ala Thr Trp Cys Phe Gly Asp Lys Val Leu Glu Thr Gly Asp Arg Val
    6930              6935              6940
Lys Met Lys Thr Leu Ser Ala Tyr Ala Glu Leu Val Ile Ser Pro Ser
6945              6950              6955              6960
Glu Arg Ser Asp Lys Gly Ile Tyr Thr Leu Lys Leu Glu Asn Arg Val
              6965              6970              6975
Lys Thr Ile Ser Gly Glu Ile Asp Val Asn Val Ile Ala Arg Pro Ser
        6980              6985              6990
Ala Pro Lys Glu Leu Lys Phe Gly Asp Ile Thr Lys Asp Ser Val His
        6995              7000              7005
Leu Thr Trp Glu Pro Pro Asp Asp Asp Gly Gly Ser Pro Leu Thr Gly
    7010              7015              7020
Tyr Val Val Glu Lys Arg Glu Val Ser Arg Lys Thr Trp Thr Lys Val
7025              7030              7035              7040
Met Asp Phe Val Thr Asp Leu Glu Phe Thr Val Pro Asp Leu Val Gln
              7045              7050              7055
Gly Lys Glu Tyr Leu Phe Lys Val Cys Ala Arg Asn Lys Cys Gly Pro
              7060              7065              7070
Gly Glu Pro Ala Tyr Val Asp Glu Pro Val Asn Met Ser Thr Pro Ala
              7075              7080              7085
Thr Val Pro Asp Pro Pro Glu Asn Val Lys Trp Arg Asp Arg Thr Ala
        7090              7095              7100
Asn Ser Ile Phe Leu Thr Trp Asp Pro Pro Lys Asn Asp Gly Gly Ser
7105              7110              7115              7120
Arg Ile Lys Gly Tyr Ile Val Glu Arg Cys Pro Arg Gly Ser Asp Lys
              7125              7130              7135
Trp Val Ala Cys Gly Glu Pro Val Ala Glu Thr Lys Met Glu Val Thr
        7140              7145              7150
Gly Leu Glu Glu Gly Lys Trp Tyr Ala Tyr Arg Val Lys Thr Leu Asn
        7155              7160              7165
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Arg Gln Gly Ala Ser Lys Pro Ser Arg Pro Thr Glu Glu Ile Gln Ala
    7170                7175            7180
Val Asp Thr Gln Glu Ala Pro Glu Ile Phe Leu Asp Val Lys Leu Leu
7185                7190            7195                7200
Ala Gly Leu Thr Val Lys Ala Gly Thr Lys Ile Glu Leu Pro Ala Thr
            7205            7210            7215
Val Thr Gly Lys Pro Glu Pro Lys Ile Thr Trp Thr Lys Ala Asp Met
            7220            7225            7230
Ile Leu Lys Gln Asp Lys Arg Ile Thr Ile Glu Asn Val Pro Lys Lys
        7235            7240            7245
Ser Thr Val Thr Ile Val Asp Ser Lys Arg Ser Asp Thr Gly Thr Tyr
    7250            7255            7260
Ile Ile Glu Ala Val Asn Val Cys Gly Arg Ala Thr Ala Val Val Glu
7265            7270            7275                7280
Val Asn Val Leu Asp Lys Pro Gly Pro Pro Ala Ala Phe Asp Ile Thr
            7285            7290            7295
Asp Val Thr Asn Glu Ser Cys Leu Leu Thr Trp Asn Pro Pro Arg Asp
            7300            7305            7310
Asp Gly Gly Ser Lys Ile Thr Asn Tyr Val Val Glu Arg Arg Ala Thr
    7315            7320            7325
Asp Ser Glu Val Trp His Lys Leu Ser Ser Thr Val Lys Asp Thr Asn
    7330            7335            7340
Phe Lys Ala Thr Lys Leu Ile Pro Asn Lys Glu Tyr Ile Phe Arg Val
7345            7350            7355                7360
Ala Ala Glu Asn Met Tyr Gly Ala Gly Glu Pro Val Gln Ala Ser Pro
            7365            7370            7375
Ile Thr Ala Lys Tyr Gln Phe Asp Pro Pro Gly Pro Pro Thr Arg Leu
        7380            7385            7390
Glu Pro Ser Asp Ile Thr Lys Asp Ala Val Thr Leu Thr Trp Cys Glu
    7395            7400            7405
Pro Asp Asp Asp Gly Gly Ser Pro Ile Thr Gly Tyr Trp Val Glu Arg
    7410            7415            7420
Leu Asp Pro Asp Thr Asp Lys Trp Val Arg Cys Asn Lys Met Pro Val
7425            7430            7435                . 7440
Lys Asp Thr Thr Tyr Arg Val Lys Gly Leu Thr Asn Lys Lys Lys Tyr
            7445            7450            7455
Arg Phe Arg Val Leu Ala Glu Asn Leu Ala Gly Pro Gly Lys Pro Ser
        7460            7465            7470
Lys Ser Thr Glu Pro Ile Leu Ile Lys Asp Pro Ile Asp Pro Pro Trp
    7475            7480            7485
Pro Pro Gly Lys Pro Thr Val Lys Asp Val Gly Lys Thr Ser Val Arg
    7490            7495            7500
Leu Asn Trp Thr Lys Pro Glu His Asp Gly Gly Ala Lys Ile Glu Ser
7505            . 7510            7515                7520
Tyr Val Ile Glu Met Leu Lys Thr Gly Thr Asp Glu Trp Val Arg Val
            7525            7530            7535
Ala Glu Gly Val Pro Thr Thr Gln His Leu Leu Pro Gly Leu Met Glu
            7540            7545            7550
Gly Gln Glu Tyr Ser Phe Arg Val Arg Ala Val Asn Lys Ala Gly Glu
    7555            7560            7565
Ser Glu Pro Ser Glu Pro Ser Asp Pro Val Leu Cys Arg Glu Lys Leu
    7570            7575            7580
Tyr Pro Pro Ser Pro Pro Arg Trp Leu Glu Val Ile Asn Ile Thr Lys
7585            7590            7595                7600
Asn Thr Ala Asp Leu Lys Trp Thr Val Pro Glu Lys Asp Gly Gly Ser
            7605            7610            7615
Pro Ile Thr Asn Tyr Ile Val Glu Lys Arg Asp Val Arg Arg Lys Gly
        7620            7625            7630
Trp Gln Thr Val Asp Thr Thr Val Lys Asp Thr Lys Cys Thr Val Thr
        7635            7640            7645
Pro Leu Thr Glu Gly Ser Leu Tyr Val Phe Arg Val Ala Ala Glu Asn
    7650            7655            7660
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Ala Ile Gly Gln Ser Asp Tyr Thr Glu Ile Glu Asp Ser Val Leu Ala
7665                7670                7675                7680
Lys Asp Thr Phe Thr Thr Pro Gly Pro Pro Tyr Ala Leu Ala Val Val
                7685                7690                7695
Asp Val Thr Lys Arg His Val Asp Leu Lys Trp Glu Pro Pro Lys Asn
                7700                7705                7710
Asp Gly Gly Arg Pro Ile Gln Arg Tyr Val Ile Glu Lys Lys Glu Arg
                7715                7720                7725
Leu Gly Thr Arg Trp Val Lys Ala Gly Lys Thr Ala Gly Pro Asp Cys
                7730                7735                7740
Asn Phe Arg Val Thr Asp Val Ile Glu Gly Thr Glu Val Gln Phe Gln
7745                7750                7755                7760
Val Arg Ala Glu Asn Glu Ala Gly Val Gly His Pro Ser Glu Pro Thr
                7765                7770                7775
Glu Ile Leu Ser Ile Glu Asp Pro Thr Ser Pro Pro Ser Pro Pro Leu
                7780                7785                7790
Asp Leu His Val Thr Asp Ala Gly Arg Lys His Ile Ala Ile Ala Trp
                7795                7800                7805
Lys Pro Pro Glu Lys Asn Gly Gly Ser Pro Ile Ile Gly Tyr His Val
                7810                7815                7820
Glu Met Cys Pro Val Gly Thr Glu Lys Trp Met Arg Val Asn Ser Arg
7825                7830                7835                7840
Pro Ile Lys Asp Leu Lys Phe Lys Val Glu Glu Gly Val Val Pro Asp
                7845                7850                7855
Lys Glu Tyr Val Leu Arg Val Arg Ala Val Asn Ala Ile Gly Val Ser
                7860                7865                7870
Glu Pro Ser Glu Ile Ser Glu Asn Val Val Ala Lys Asp Pro Asp Cys
                7875                7880                7885
Lys Pro Thr Ile Asp Leu Glu Thr His Asp Ile Ile Val Ile Glu Gly
                7890                7895                7900
Glu Lys Leu Ser Ile Pro Val Pro Phe Arg Ala Val Pro Val Pro Thr
7905                7910                7915                7920
Val Ser Trp His Lys Asp Gly Lys Glu Val Lys Ala Ser Asp Arg Leu
                7925                7930                7935
Thr Met Lys Asn Asp His Ile Ser Ala His Leu Glu Val Pro Lys Ser
                7940                7945                7950
Val Arg Ala Asp Ala Gly Ile Tyr Thr Ile Thr Leu Glu Asn Lys Leu
                7955                7960                7965
Gly Ser Ala Thr Ala Ser Ile Asn Val Lys Val Ile Gly Leu Pro Gly
7970                7975                7980
Pro Cys Lys Asp Ile Lys Ala Ser Asp Ile Thr Lys Ser Ser Cys Lys
7985                7990                7995                8000
Leu Thr Trp Glu Pro Pro Glu Phe Asp Gly Gly Thr Pro Ile Leu His
                8005                8010                8015
Tyr Val Leu Glu Arg Arg Glu Ala Gly Arg Arg Thr Tyr Ile Pro Val
                8020                8025                8030
Met Ser Gly Glu Asn Lys Leu Ser Trp Thr Val Lys Asp Leu Ile Pro
                8035                8040                8045
Asn Gly Glu Tyr Phe Phe Arg Val Lys Ala Val Asn Lys Val Gly Gly
                8050                8055                8060
Gly Glu Tyr Ile Glu Leu Lys Asn Pro Val Ile Ala Gln Asp Pro Lys
8065                8070                8075                8080
Gln Pro Pro Asp Pro Pro Val Asp Val Glu Val His Asn Pro Thr Ala
                8085                8090                8095
Glu Ala Met Thr Ile Thr Trp Lys Pro Pro Leu Tyr Asp Gly Gly Ser
                8100                8105                8110
Lys Ile Met Gly Tyr Ile Ile Glu Lys Ile Ala Lys Gly Glu Glu Arg
                8115                8120                8125
Trp Lys Arg Cys Asn Glu His Leu Val Pro Ile Leu Thr Tyr Thr Ala
                8130                8135                8140
Lys Gly Leu Glu Glu Gly Lys Glu Tyr Gln Phe Arg Val Arg Ala Glu
8145                8150                8155                8160
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Asn Ala Ala Gly Ile Ser Glu Pro Ser Arg Ala Thr Pro Pro Thr Lys
              8165                8170                8175
Ala Val Asp Pro Ile Asp Ala Pro Lys Val Ile Leu Arg Thr Ser Leu
              8180                8185                8190
Glu Val Lys Arg Gly Asp Glu Ile Ala Leu Asp Ala Ser Ile Ser Gly
         8195                8200                8205
Ser Pro Tyr Pro Thr Ile Thr Trp Ile Lys Asp Glu Asn Val Ile Val
    8210                8215                8220
Pro Glu Glu Ile Lys Lys Arg Ala Ala Pro Leu Val Arg Arg Arg Lys
8225                8230                8235                8240
Gly Glu Val Gln Glu Glu Pro Phe Val Leu Pro Leu Thr Gln Arg
              8245                8250                8255
Leu Ser Ile Asp Asn Ser Lys Lys Gly Glu Ser Gln Leu Arg Val Arg
              8260                8265                8270
Asp Ser Leu Arg Pro Asp His Gly Leu Tyr Met Ile Lys Val Glu Asn
         8275                8280                8285
Asp His Gly Ile Ala Lys Ala Pro Cys Thr Val Ser Val Leu Asp Thr
    8290                8295                8300
Pro Gly Pro Pro Ile Asn Phe Val Phe Glu Asp Ile Arg Lys Thr Ser
8305                8310                8315                8320
Val Leu Cys Lys Trp Glu Pro Pro Leu Asp Asp Gly Gly Ser Glu Ile
              8325                8330                8335
Ile Asn Tyr Thr Leu Glu Lys Lys Asp Lys Thr Lys Pro Asp Ser Glu
         8340                8345                8350
Trp Ile Val Val Thr Ser Thr Leu Arg His Cys Lys Tyr Ser Val Thr
    8355                8360                8365
Lys Leu Ile Glu Gly Lys Glu Tyr Leu Phe Arg Val Arg Ala Glu Asn
8370                8375                8380
Arg Phe Gly Pro Gly Pro Pro Cys Val Ser Lys Pro Leu Val Ala Lys
8385                8390                8395                8400
Asp Pro Phe Gly Pro Pro Asp Ala Pro Asp Lys Pro Ile Val Glu Asp
         8405                8410                8415
Val Thr Ser Asn Ser Met Leu Val Lys Trp Asn Glu Pro Lys Asp Asn
         8420                8425                8430
Gly Ser Pro Ile Leu Gly Tyr Trp Leu Glu Lys Arg Glu Val Asn Ser
    8435                8440                8445
Thr His Trp Ser Arg Val Asn Lys Ser Leu Leu Asn Ala Leu Lys Ala
    8450                8455                8460
Asn Val Asp Gly Leu Leu Glu Gly Leu Thr Tyr Val Phe Arg Val Cys
8465                8470                8475                8480
Ala Glu Asn Ala Ala Gly Pro Gly Lys Phe Ser Pro Pro Ser Asp Pro
         8485                8490                8495
Lys Thr Ala His Asp Pro Ile Ser Pro Pro Gly Pro Pro Ile Pro Arg
         8500                8505                8510
Val Thr Asp Thr Ser Ser Thr Thr Ile Glu Leu Glu Trp Glu Pro Pro
    8515                8520                8525
Ala Phe Asn Gly Gly Gly Glu Ile Val Gly Tyr Phe Val Asp Lys Gln
    8530                8535                8540
Leu Val Gly Thr Asn Lys Trp Ser Arg Cys Thr Glu Lys Met Ile Lys
8545                8550                8555                8560
Val Arg Gln Tyr Thr Val Lys Glu Ile Arg Glu Gly Ala Asp Tyr Lys
         8565                8570                8575
Leu Arg Val Ser Ala Val Asn Ala Ala Gly Glu Gly Pro Pro Gly Glu
         8580                8585                8590
Thr Gln Pro Val Thr Val Ala Glu Pro Gln Glu Pro Pro Ala Val Glu
    8595                8600                8605
Leu Asp Val Ser Val Lys Gly Gly Ile Gln Ile Met Ala Gly Lys Thr
    8610                8615                8620
Leu Arg Ile Pro Ala Val Val Thr Gly Arg Pro Val Pro Thr Lys Val
8625                8630                8635                8640
Trp Thr Lys Glu Glu Gly Glu Leu Asp Lys Asp Arg Val Val Ile Asp
              8645                8650                8655
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Asn Val Gly Thr Lys Ser Glu Leu Ile Ile Lys Asp Ala Leu Arg Lys
             8660                8665                8670
Asp His Gly Arg Tyr Val Ile Thr Ala Thr Asn Ser Cys Gly Ser Lys
         8675                8680                8685
Phe Ala Ala Ala Arg Val Glu Val Phe Asp Val Pro Gly Pro Val Leu
     8690                8695                8700
Asp Leu Lys Pro Val Val Thr Asn Arg Lys Met Cys Leu Leu Asn Trp
8705                8710                8715                8720
Ser Asp Pro Glu Asp Asp Gly Gly Ser Glu Ile Thr Gly Phe Ile Ile
             8725                8730                8735
Glu Arg Lys Asp Ala Lys Met His Thr Trp Arg Gln Pro Ile Glu Thr
             8740                8745                8750
Glu Arg Ser Lys Cys Asp Ile Thr Gly Leu Leu Glu Gly Gln Glu Tyr
         8755                8760                8765
Lys Phe Arg Val Ile Ala Lys Asn Lys Phe Gly Cys Gly Pro Pro Val
     8770                8775                8780
Glu Ile Gly Pro Ile Leu Ala Val Asp Pro Leu Gly Pro Pro Thr Ser
8785                8790                8795                8800
Pro Glu Arg Leu Thr Tyr Thr Glu Arg Gln Arg Ser Thr Ile Thr Leu
             8805                8810                8815
Asp Trp Lys Glu Pro Arg Ser Asn Gly Gly Ser Pro Ile Gln Gly Tyr
             8820                8825                8830
Ile Ile Glu Lys Arg Arg His Asp Lys Pro Asp Phe Glu Arg Val Asn
         8835                8840                8845
Lys Arg Leu Cys Pro Thr Thr Ser Phe Leu Val Glu Asn Leu Asp Glu
     8850                8855                8860
His Gln Met Tyr Glu Phe Arg Val Lys Ala Val Asn Glu Ile Gly Glu
8865                8870                8875                8880
Ser Glu Pro Ser Leu Pro Leu Asn Val Val Ile Gln Asp Asp Glu Val
             8885                8890                8895
Pro Pro Thr Ile Lys Leu Arg Leu Ser Val Arg Gly Asp Thr Ile Lys
             8900                8905                8910
Val Lys Ala Gly Glu Pro Val His Ile Pro Ala Asp Val Thr Gly Leu
     8915                8920                8925
Pro Met Pro Lys Ile Glu Trp Ser Lys Asn Glu Thr Val Ile Glu Lys
     8930                8935                8940
Pro Thr Asp Ala Leu Gln Ile Thr Lys Glu Glu Val Ser Arg Ser Glu
8945                8950                8955                8960
Ala Lys Thr Glu Leu Ser Ile Pro Lys Ala Val Arg Glu Asp Lys Gly
             8965                8970                8975
Thr Tyr Thr Val Thr Ala Ser Asn Arg Leu Gly Ser Val Phe Arg Asn
         8980                8985                8990
Val His Val Glu Val Tyr Asp Arg Pro Ser Pro Arg Asn Leu Ala
     8995                9000                9005
Val Thr Asp Ile Lys Ala Glu Ser Cys Tyr Leu Thr Trp Asp Ala Pro
     9010                9015                9020
Leu Asp Asn Gly Gly Ser Glu Ile Thr His Tyr Val Ile Asp Lys Arg
9025                9030                9035                9040
Asp Ala Ser Arg Lys Lys Ala Glu Trp Glu Glu Val Thr Asn Thr Ala
             9045                9050                9055
Val Glu Lys Arg Tyr Gly Ile Trp Lys Leu Ile Pro Asn Gly Gln Tyr
         9060                9065                9070
Glu Phe Arg Val Arg Ala Val Asn Lys Tyr Gly Ile Ser Asp Glu Cys
     9075                9080                9085
Lys Ser Asp Lys Val Val Ile Gln Asp Pro Tyr Arg Leu Pro Gly Pro
     9090                9095                9100
Pro Gly Lys Pro Lys Val Leu Ala Arg Thr Lys Gly Ser Met Leu Val
9105                9110                9115                9120
Ser Trp Thr Pro Pro Leu Asp Asn Gly Gly Ser Pro Ile Thr Gly Tyr
             9125                9130                9135
Trp Leu Glu Lys Arg Glu Glu Gly Ser Pro Tyr Trp Ser Arg Val Ser.
             9140                9145                9150
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Arg Ala Pro Ile Thr Lys Val Gly Leu Lys Gly Val Glu Phe Asn Val
    9155                9160                9165
Pro Arg Leu Leu Glu Gly Val Lys Tyr Gln Phe Arg Ala Met Ala Ile
    9170                9175                9180
Asn Ala Ala Gly Ile Gly Pro Pro Ser Glu Pro Ser Asp Pro Glu Val
9185                9190                9195                9200
Ala Gly Asp Pro Ile Phe Pro Pro Gly Pro Pro Ser Cys Pro Glu Val
                9205                9210                9215
Lys Asp Lys Thr Lys Ser Ser Ile Ser Leu Gly Trp Lys Pro Pro Ala
                9220                9225                9230
Lys Asp Gly Gly Ser Pro Ile Lys Gly Tyr Ile Val Glu Met Gln Glu
                9235                9240                9245
Glu Gly Thr Thr Asp Trp Lys Arg Val Asn Glu Pro Asp Lys Leu Ile
                9250                9255                9260
Thr Thr Cys Glu Cys Val Val Pro Asn Leu Lys Glu Leu Arg Lys Tyr
9265                9270                9275                9280
Arg Phe Arg Val Lys Ala Val Asn Glu Ala Gly Glu Ser Glu Pro Ser
                9285                9290                9295
Asp Thr Thr Gly Glu Ile Pro Ala Thr Asp Ile Gln Glu Glu Pro Glu
                9300                9305                9310
Val Phe Ile Asp Ile Gly Ala Gln Asp Cys Leu Val Cys Lys Ala Gly
                9315                9320                9325
Ser Gln Ile Arg Ile Pro Ala Val Ile Lys Gly Arg Pro Thr Pro Lys
                9330                9335                9340
Ser Ser Trp Glu Phe Asp Gly Lys Ala Lys Lys Ala Met Lys Asp Gly
9345                9350                9355                9360
Val His Asp Ile Pro Glu Asp Ala Gln Leu Glu Thr Ala Glu Asn Ser
                9365                9370                9375
Ser Val Ile Ile Ile Pro Glu Cys Lys Arg Ser His Thr Gly Lys Tyr
                9380                9385                9390
Ser Ile Thr Ala Lys Asn Lys Ala Gly Gln Lys Thr Ala Asn Cys Arg
                9395                9400                9405
Val Lys Val Met Asp Val Pro Gly Pro Pro Lys Asp Leu Lys Val Ser
                9410                9415                9420
Asp Ile Thr Arg Gly Ser Cys Arg Leu Ser Trp Lys Met Pro Asp Asp
9425                9430                9435                9440
Asp Gly Gly Asp Arg Ile Lys Gly Tyr Val Ile Glu Lys Arg Thr Ile
                9445                9450                9455
Asp Gly Lys Ala Trp Thr Lys Val Asn Pro Asp Cys Gly Ser Thr Thr
                9460                9465                9470
Phe Val Val Pro Asp Leu Leu Ser Glu Gln Gln Tyr Phe Phe Arg Val
                9475                9480                9485
Arg Ala Glu Asn Arg Phe Gly Ile Gly Pro Pro Val Glu Thr Ile Gln
    9490                9495                9500
Arg Thr Thr Ala Arg Asp Pro Ile Tyr Pro Pro Asp Pro Pro Ile Lys
9505                9510                9515                9520
Leu Lys Ile Gly Leu Ile Thr Lys Asn Thr Val His Leu Ser Trp Lys
                9525                9530                9535
Pro Pro Lys Asn Asp Gly Gly Ser Pro Val Thr His Tyr Ile Val Glu
                9540                9545                9550
Cys Leu Ala Trp Asp Pro Thr Gly Thr Lys Lys Glu Ala Trp Arg Gln
    9555                9560                9565
Cys Asn Lys Arg Asp Val Glu Glu Leu Gln Phe Thr Val Glu Asp Leu
9570                9575                9580
Val Glu Gly Gly Glu Tyr Glu Phe Arg Val Lys Ala Val Asn Ala Ala
9585                9590                9595                9600
Gly Val Ser Lys Pro Ser Ala Thr Val Gly Pro Cys Asp Cys Gln Arg
                9605                ·9610                9615
Pro Asp Met Pro Pro Ser Ile Asp Leu Lys Glu Phe Met Glu Val Glu
                9620                9625                9630
Glu Gly Thr Asn Val Asn Ile Val Ala Lys Ile Lys Gly Val Pro Phe
                9635                9640                9645
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Pro Thr Leu Thr Trp Phe Lys Ala Pro Pro Lys Lys Pro Asp Asn Lys
    9650   9655   9660
Glu Pro Val Leu Tyr Asp Thr His Val Asn Lys Leu Val Val Asp Asp
9665   9670   9675   9680
Thr Cys Thr Leu Val Ile Pro Gln Ser Arg Arg Ser Asp Thr Gly Leu
            9685   9690   9695
Tyr Thr Ile Thr Ala Val Asn Asn Leu Gly Thr Ala Ser Lys Glu Met
            9700   9705   9710
Arg Leu Asn Val Leu Gly Arg Pro Gly Pro Pro Val Gly Pro Ile Lys
    9715   9720   9725
Phe Glu Ser Val Ser Ala Asp Gln Met Thr Leu Ser Trp Phe Pro Pro
    9730   9735   9740
Lys Asp Asp Gly Gly Ser Lys Ile Thr Asn Tyr Val Ile Glu Lys Arg
9745   9750   9755   9760
Glu Ala Asn Arg Lys Thr Trp Val His Val Ser Ser Glu Pro Lys Glu
            9765   9770   9775
Cys Thr Tyr Thr Ile Pro Lys Leu Leu Glu Gly His Glu Tyr Val Phe
            9780   9785   9790
Arg Ile Met Ala Gln Asn Lys Tyr Gly Ile Gly Glu Pro Leu Asp Ser
    9795   9800   9805
Glu Pro Glu Thr Ala Arg Asn Leu Phe Ser Val Pro Gly Ala Pro Asp
    9810   9815   9820
Lys Pro Thr Val Ser Ser Val Thr Arg Asn Ser Met Thr Val Asn Trp
9825   9830   9835   9840
Glu Glu Pro Glu Tyr Asp Gly Gly Ser Pro Val Thr Gly Tyr Trp Leu
            9845   9850   9855
Glu Met Lys Asp Thr Thr Ser Lys Arg Trp Lys Arg Val Asn Arg Asp
        9860   9865   9870
Pro Ile Lys Ala Met Thr Leu Gly Val Ser Tyr Lys Val Thr Gly Leu
            9875   9880   9885
Ile Glu Gly Ser Asp Tyr Gln Phe Arg Val Tyr Ala Ile Asn Ala Ala
    9890   9895   9900
Gly Val Gly Pro Ala Ser Leu Pro Ser Asp Pro Ala Thr Ala Arg Asp
9905   9910   9915   9920
Pro Ile Ala Pro Gly Pro Pro Phe Pro Lys Val Thr Asp Trp Thr
            9925   9930   9935
Lys Ser Ser Ala Asp Leu Glu Trp Ser Pro Pro Leu Lys Asp Gly Gly
        9940   9945   9950
Ser Lys Val Thr Gly Tyr Ile Val Glu Tyr Lys Glu Glu Gly Lys Glu
    9955   9960   9965
Glu Trp Glu Lys Gly Lys Asp Lys Glu Val Arg Gly Thr Lys Leu Val
    9970   9975   9980
Val Thr Gly Leu Lys Glu Gly Ala Phe Tyr Lys Phe Arg Val Ser Ala
9985   9990   9995   10000
Val Asn Ile Ala Gly Ile Gly Glu Pro Gly Glu Val Thr Asp Val Ile
            10005   10010   10015
Glu Met Lys Asp Arg Leu Val Ser Pro Asp Leu Gln Leu Asp Ala Ser
            10020   10025   10030
Val Arg Asp Arg Ile Val Val His Ala Gly Gly Val Ile Arg Ile Ile
        10035   10040   10045
Ala Tyr Val Ser Gly Lys Pro Pro Pro Thr Val Thr Trp Asn Met Asn
    10050   10055   10060   1
Glu Arg Thr Leu Pro Gln Glu Ala Thr Ile Glu Thr Thr Ala Ile Ser
0065   10070   10075   10080
Ser Ser Met Val Ile Lys Asn Cys Gln Arg Ser His Gln Gly Val Tyr
            10085   10090   10095
Ser Leu Leu Ala Lys Asn Glu Ala Gly Glu Arg Lys Lys Thr Ile Ile
            10100   10105   10110
Val Asp Val Leu Asp Val Pro Gly Pro Val Gly Thr Pro Phe Leu Ala
        10115   10120   10125
His Asn Leu Thr Asn Glu Ser Cys Lys Leu Thr Trp Phe Ser Pro Glu
    10130   10135   10140   1

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Asp Asp Gly Gly Ser Pro Ile Thr Asn Tyr Val Ile Glu Lys Arg Glu
0145            10150            10155                 10160
Ser Asp Arg Arg Ala Trp Thr Pro Val Thr Tyr Thr Val Thr Arg Gln
          10165            10170            10175
Asn Ala Thr Val Gln Gly Leu Ile Gln Gly Lys Ala Tyr Phe Phe Arg
            10180            10185            10190
Ile Ala Ala Glu Asn Ser Ile Gly Met Gly Pro Phe Val Glu Thr Ser
          10195            10200            10205
Glu Ala Leu Val Ile Arg Glu Pro Ile Thr Val Pro Glu Arg Pro Glu
  10210            10215            10220                      1
Asp Leu Glu Val Lys Glu Val Thr Lys Asn Thr Val Thr Leu Thr Trp
0225            10230            10235            10240
Asn Pro Pro Lys Tyr Asp Gly Gly Ser Glu Ile Ile Asn Tyr Val Leu
          10245            10250            10255
Glu Ser Arg Leu Ile Gly Thr Glu Lys Phe His Lys Val Thr Asn Asp
            10260            10265            10270
Asn Leu Leu Ser Arg Lys Tyr Thr Val Lys Gly Leu Lys Glu Gly Asp
          10275            10280            10285
Thr Tyr Glu Tyr Arg Val Ser Ala Val Asn Ile Val Gly Gln Gly Lys
  10290            10295            10300                      1
Pro Ser Phe Cys Thr Lys Pro Ile Thr Cys Lys Asp Glu Leu Ala Pro
0305            10310            10315            10320
Pro Thr Leu His Leu Asp Phe Arg Asp Lys Leu Thr Ile Arg Val Gly
          10325            10330            10335
Glu Ala Phe Ala Leu Thr Gly Arg Tyr Ser Gly Lys Pro Lys Pro Lys
  10340            10345            10350
Val Ser Trp Phe Lys Asp Glu Ala Asp Val Leu Glu Asp Asp Arg Thr
          10355            10360            10365
His Ile Lys Thr Thr Pro Ala Thr Leu Ala Leu Glu Lys Ile Lys Ala
  10370            10375            10380                      1
Lys Arg Ser Asp Ser Gly Lys Tyr Cys Val Val Val Glu Asn Ser Thr
0385            10390            10395            10400
Gly Ser Arg Lys Gly Phe Cys Gln Val Asn Val Val Asp His Pro Gly
          10405            10410            10415
Pro Pro Val Gly Pro Val Ser Phe Asp Glu Val Thr Lys Asp Tyr Met
          10420            10425            10430
Val Ile Ser Trp Lys Pro Pro Leu Asp Asp Gly Gly Ser Lys Ile Thr
          10435            10440            10445
Asn Tyr Ile Ile Glu Lys Lys Glu Val Gly Lys Asp Val Trp Met Pro
  10450            10455            10460                      1
Val Thr Ser Ala Ser Ala Lys Thr Thr Cys Lys Val Ser Lys Leu Leu
0465            10470            10475            10480
Glu Gly Lys Asp Tyr Ile Phe Arg Ile His Ala Glu Asn Leu Tyr Gly
          10485            10490            10495
Ile Ser Asp Pro Leu Val Ser Asp Ser Met Lys Ala Lys Asp Arg Phe
          10500            10505            10510
Arg Val Pro Asp Ala Pro Asp Gln Pro Ile Val Thr Glu Val Thr Lys
          10515            10520            10525
Asp Ser Ala Leu Val Thr Trp Asn Lys Pro His Asp Gly Gly Lys Pro
  10530            10535            10540                      1
Ile Thr Asn Tyr Ile Leu Glu Lys Arg Glu Thr Met Ser Lys Arg Trp
0545            10550            10555            10560
Ala Arg Val Thr Lys Asp Pro Ile His Pro Tyr Thr Lys Phe Arg Val
          10565            10570            10575
Pro Asp Leu Leu Glu Gly Cys Gln Tyr Glu Phe Arg Val Ser Ala Glu
          10580            10585            10590
Asn Glu Ile Gly Ile Gly Asp Pro Ser Pro Pro Ser Lys Pro Val Phe
  10595            10600            10605
Ala Lys Asp Pro Ile Ala Lys Pro Ser Pro Val Asn Pro Glu Ala
  10610            10615            10620                      1
Ile Asp Thr Thr Cys Asn Ser Val Asp Leu Thr Trp Gln Pro Pro Arg
0625            10630            10635                 10640
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His Asp Gly Gly Ser Lys Ile Leu Gly Tyr Ile Val Glu Tyr Gln Lys
        10645                   10650                   10655
Val Gly Asp Glu Glu Trp Arg Arg Ala Asn His Thr Pro Glu Ser Cys
        10660                   10665                   10670
Pro Glu Thr Lys Tyr Lys Val Thr Gly Leu Arg Asp Gly Gln Thr Tyr
        10675                   10680                   10685
Lys Phe Arg Val Leu Ala Val Asn Ala Ala Gly Glu Ser Asp Pro Ala
     10690                   10695                   10700           1
His Val Pro Glu Pro Val Leu Val Lys Asp Arg Leu Glu Pro Pro Glu
0705             10710                   10715               10720
Leu Ile Leu Asp Ala Asn Met Ala Arg Glu Gln His Ile Lys Val Gly
             10725                   10730                   10735
Asp Thr Leu Arg Leu Ser Ala Ile Ile Lys Gly Val Pro Phe Pro Lys
             10740                   10745                   10750
Val Thr Trp Lys Lys Glu Asp Arg Asp Ala Pro Thr Lys Ala Arg Ile
        10755                   10760                   10765
Asp Val Thr Pro Val Gly Ser Lys Leu Glu Ile Arg Asn Ala Ala His
     10770                   10775                   10780           1
Glu Asp Gly Gly Ile Tyr Ser Leu Thr Val Glu Asn Pro Ala Gly Ser
0785             10790                   10795               10800
Lys Thr Val Ser Val Lys Val Leu Val Leu Asp Lys Pro Gly Pro Pro
             10805                   10810               10815
Arg Asp Leu Glu Val Ser Glu Ile Arg Lys Asp Ser Cys Tyr Leu Thr
             10820                   10825                   10830
Trp Lys Glu Pro Leu Asp Asp Gly Gly Ser Val Ile Thr Asn Tyr Val
        10835                   10840                   10845
Val Glu Arg Arg Asp Val Ala Ser Ala Gln Trp Ser Pro Leu Ser Ala
     10850                   10855               10860               1
Thr Ser Lys Lys Lys Ser His Phe Ala Lys His Leu Asn Glu Gly Asn
0865             10870                   10875               10880
Gln Tyr Leu Phe Arg Val Ala Ala Glu Asn Gln Tyr Gly Arg Gly Pro
             10885                   10890                   10895
Phe Val Glu Thr Pro Lys Pro Ile Lys Ala Leu Asp Pro Leu His Pro
        10900                   10905                   10910
Pro Gly Pro Pro Lys Asp Leu His Val Asp Val Asp Lys Thr Glu
        10915                   10920                   10925
Val Ser Leu Val Trp Asn Lys Pro Asp Arg Asp Gly Gly Ser Pro Ile
     10930                   10935                   10940           1
Thr Gly Tyr Leu Val Glu Tyr Gln Glu Glu Gly Thr Gln Asp Trp Ile
0945             10950                   10955                   10960
Lys Phe Lys Thr Val Thr Asn Leu Glu Cys Val Val Thr Gly Leu Gln
        10965                   10970                   10975
Gln Gly Lys Thr Tyr Arg Phe Arg Val Lys Ala Glu Asn Ile Val Gly
        10980                   10985                   10990
Leu Gly Leu Pro Asp Thr Thr Ile Pro Ile Glu Cys Gln Glu Lys Leu
        10995                   11000                   11005
Val Pro Pro Ser Val Glu Leu Asp Val Lys Leu Ile Glu Gly Leu Val
     11010                   11015                   11020           1
Val Lys Ala Gly Thr Thr Val Arg Phe Pro Ala Ile Ile Arg Gly Val
1025             11030                   11035                   11040
Pro Val Pro Thr Ala Lys Trp Thr Thr Asp Gly Ser Glu Ile Lys Thr
             11045                   11050                   11055
Asp Glu His Tyr Thr Val Glu Thr Asp Asn Phe Ser Ser Val Leu Thr
             11060                   11065                   11070
Ile Lys Asn Cys Leu Arg Arg Asp Thr Gly Glu Tyr Gln Ile Thr Val
        11075                   11080                   11085
Ser Asn Ala Ala Gly Ser Lys Thr Val Ala Val His Leu Thr Val Leu
     11090                   11095                   11100           1
Asp Val Pro Gly Pro Pro Thr Gly Pro Ile Asn Ile Leu Asp Val Thr
1105             11110                   11115                   11120
Pro Glu His Met Thr Ile Ser Trp Gln Pro Pro Lys Asp Asp Gly Gly
             11125                   11130                   11135
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Ser Pro Val Ile Asn Tyr Ile Val Glu Lys Gln Asp Thr Arg Lys Asp
         11140                 11145                 11150
Thr Trp Gly Val Val Ser Ser Gly Ser Ser Lys Thr Lys Leu Lys Ile
         11155                 11160                 11165
Pro His Leu Gln Lys Gly Cys Glu Tyr Val Phe Arg Val Arg Ala Glu
      11170               11175                 11180              1
Asn Lys Ile Gly Val Gly Pro Pro Leu Asp Ser Thr Pro Thr Val Ala
   1185               11190                 11195                 11200
Lys His Lys Phe Ser Pro Pro Ser Pro Pro Gly Lys Pro Val Val Thr
              11205                 11210                 11215
Asp Ile Thr Glu Asn Ala Ala Thr Val Ser Trp Thr Leu Pro Lys Ser
         11220                 11225                 11230
Asp Gly Gly Ser Pro Ile Thr Gly Tyr Tyr Met Glu Arg Arg Glu Val
         11235                 11240                 11245
Thr Gly Lys Trp Val Arg Val Asn Lys Thr Pro Ile Ala Asp Leu Lys
      11250                 11255                 11260          1
Phe Arg Val Thr Gly Leu Tyr Glu Gly Asn Thr Tyr Glu Phe Arg Val
   1265               11270                 11275                 11280
Phe Ala Glu Asn Leu Ala Gly Leu Ser Lys Pro Ser Pro Ser Ser Asp
         11285                 11290                 11295
Pro Ile Lys Ala Cys Arg Pro Ile Lys Pro Pro Gly Pro Pro Ile Asn
         11300                 11305                 11310
Pro Lys Leu Lys Asp Lys Ser Arg Glu Thr Ala Asp Leu Val Trp Thr
      11315                 11320                 11325
Lys Pro Leu Ser Asp Gly Gly Ser Pro Ile Leu Gly Tyr Val Val Glu
      11330                 11335                 11340             1
Cys Gln Lys Pro Gly Thr Ala Gln Trp Asn Arg Ile Asn Lys Asp Glu
   1345               11350                 11355                 11360
Leu Ile Arg Gln Cys Ala Phe Arg Val Pro Gly Leu Ile Glu Gly Asn
              11365                 11370                 11375
Glu Tyr Arg Phe Arg Ile Lys Ala Ala Asn Ile Val Gly Glu Gly Glu
         11380                 11385                 11390
Pro Arg Glu Leu Ala Glu Ser Val Ile Ala Lys Asp Ile Leu His Pro
      11395                 11400                 11405
Pro Glu Val Glu Leu Asp Val Thr Cys Arg Asp Val Ile Thr Val Arg
      11410                 11415                 11420             1
Val Gly Gln Thr Ile Arg Ile Leu Ala Arg Val Lys Gly Arg Pro Glu
   1425               11430                 11435                 11440
Pro Asp Ile Thr Trp Thr Lys Glu Gly Lys Val Leu Val Arg Glu Lys
              11445                 11450                 11455
Arg Val Asp Leu Ile Gln Asp Leu Pro Arg Val Glu Leu Gln Ile Lys
         11460                 11465                 11470
Glu Ala Val Arg Ala Asp His Gly Lys Tyr Ile Ile Ser Ala Lys Asn
      11475                 11480                 11485
Ser Ser Gly His Ala Gln Gly Ser Ala Ile Val Asn Val Leu Asp Arg
   11490                 11495                 11500             1
Pro Gly Pro Cys Gln Asn Leu Lys Val Thr Asn Val Thr Lys Glu Asn
   1505               11510                 11515                 11520
Cys Thr Ile Ser Trp Glu Asn Pro Leu Asp Asn Gly Gly Ser Glu Ile
              11525                 11530                 11535
Thr Asn Phe Ile Val Glu Tyr Arg Lys Pro Asn Gln Lys Gly Trp Ser
         11540                 11545                 11550
Ile Val Ala Ser Asp Val Thr Lys Arg Leu Ile Lys Ala Asn Leu Leu
      11555                 11560                 11565
Ala Asn Asn Glu Tyr Tyr Phe Arg Val Cys Ala Glu Asn Lys Val Gly
   11570                 11575                 11580             1
Val Gly Pro Thr Ile Glu Thr Lys Thr Pro Ile Leu Ala Ile Asn Pro
   1585               11590                 11595                 11600
Ile Asp Arg Pro Gly Glu Pro Glu Asn Leu His Ile Ala Asp Lys Gly
              11605                 11610                 11615
Lys Thr Phe Val Tyr Leu Lys Trp Arg Arg Pro Asp Tyr Asp Gly Gly
         11620                 11625                 11630
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Ser Pro Asn Leu Ser Tyr His Val Glu Arg Arg Leu Lys Gly Ser Asp
    11635               11640               11645
Asp Trp Glu Arg Val His Lys Gly Ser Ile Lys Glu Thr His Tyr Met
  11650               11655               11660               1
Val Asp Arg Cys Val Glu Asn Gln Ile Tyr Glu Phe Arg Val Gln Thr
1665               11670               11675               11680
Lys Asn Glu Gly Gly Glu Ser Asp Trp Val Lys Thr Glu Glu Val Val
             11685               11690               11695
Val Lys Glu Asp Leu Gln Lys Pro Val Leu Asp Leu Lys Leu Ser Gly
        11700               11705               11710
Val Leu Thr Val Lys Ala Gly Asp Thr Ile Arg Leu Glu Ala Gly Val
        11715               11720               11725
Arg Gly Lys Pro Phe Pro Glu Val Ala Trp Thr Lys Asp Lys Asp Ala
    11730               11735               11740               1
Thr Asp Leu Thr Arg Ser Pro Arg Val Lys Ile Asp Thr Arg Ala Asp
1745               11750               11755               11760
Ser Ser Lys Phe Ser Leu Thr Lys Ala Lys Arg Ser Asp Gly Gly Lys
        11765               11770               11775
Tyr Val Val Thr Ala Thr Asn Thr Ala Gly Ser Phe Val Ala Tyr Ala
             11780               11785               11790
Thr Val Asn Val Leu Asp Lys Pro Gly Pro Val Arg Asn Leu Lys Ile
        11795               11800               11805
Val Asp Val Ser Ser Asp Arg Cys Thr Val Cys Trp Asp Pro Pro Glu
    11810               11815               11820               1
Asp Asp Gly Gly Cys Glu Ile Gln Asn Tyr Ile Leu Glu Lys Cys Glu
1825               11830               11835               11840
Thr Lys Arg Met Val Trp Ser Thr Tyr Ser Ala Thr Val Leu Thr Pro
             11845               11850               11855
Gly Thr Thr Val Thr Arg Leu Ile Glu Gly Asn Glu Tyr Ile Phe Arg
        11860               11865               11870
Val Arg Ala Glu Asn Lys Ile Gly Thr Gly Pro Pro Thr Glu Ser Lys
    11875               11880               11885
Pro Val Ile Ala Lys Thr Lys Tyr Asp Lys Pro Gly Arg Pro Asp Pro
    11890               11895               11900               1
Pro Glu Val Thr Lys Val Ser Lys Glu Glu Met Thr Val Val Trp Asn
1905               11910               11915               11920
Pro Pro Glu Tyr Asp Gly Gly Lys Ser Ile Thr Gly Tyr Phe Leu Glu
             11925               11930               11935
Lys Lys Glu Lys His Ser Thr Arg Trp Val Pro Val Asn Lys Ser Ala
        11940               11945               11950
Ile Pro Glu Arg Arg Met Lys Val Gln Asn Leu Leu Pro Asp His Glu
    11955               11960               11965
Tyr Gln Phe Arg Val Lys Ala Glu Asn Glu Ile Gly Ile Gly Glu Pro
    11970               11975               11980               1
Ser Leu Pro Ser Arg Pro Val Val Ala Lys Asp Pro Ile Glu Pro Pro
1985               11990               11995               12000
Gly Pro Pro Thr Asn Phe Arg Val Val Asp Thr Thr Lys His Ser Ile
             12005               12010               12015
Thr Leu Gly Trp Gly Lys Pro Val Tyr Asp Gly Gly Ala Pro Ile Ile
         12020               12025               12030
Gly Tyr Val Val Glu Met Arg Pro Lys Ile Ala Asp Ala Ser Pro Asp
    12035               12040               12045
Glu Gly Trp Lys Arg Cys Asn Ala Ala Ala Gln Leu Val Arg Lys Glu
    12050               12055               12060               1
Phe Thr Val Thr Ser Leu Asp Glu Asn Gln Glu Tyr Glu Phe Arg Val
2065               12070               12075               12080
Cys Ala Gln Asn Gln Val Gly Ile Gly Arg Pro Ala Glu Leu Lys Glu
             12085               12090               12095
Ala Ile Lys Pro Lys Glu Ile Leu Glu Pro Pro Glu Ile Asp Leu Asp
        12100               12105               12110
Ala Ser Met Arg Lys Leu Val Ile Val Arg Ala Gly Cys Pro Ile Arg
    12115               12120               12125
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Leu Phe Ala Ile Val Arg Gly Arg Pro Ala Pro Lys Val Thr Trp Arg
    12130   12135   12140   1
Lys Val Gly Ile Asp Asn Val Val Arg Lys Gly Gln Val Asp Leu Val
2145   12150   12155   12160
Asp Thr Met Ala Phe Leu Val Ile Pro Asn Ser Thr Arg Asp Asp Ser
              12165   12170   12175
Gly Lys Tyr Ser Leu Thr Leu Val Asn Pro Ala Gly Glu Lys Ala Val
              12180   12185   12190
Phe Val Asn Val Arg Val Leu Asp Thr Pro Gly Pro Val Ser Asp Leu
          12195   12200   12205
Lys Val Ser Asp Val Thr Lys Thr Ser Cys His Val Ser Trp Ala Pro
    12210   12215   12220   1
Pro Glu Asn Asp Gly Gly Ser Gln Val Thr His Tyr Ile Val Glu Lys
2225   12230   12235   12240 .
Arg Glu Ala Asp Arg Lys Thr Trp Ser Thr Val Thr Pro Glu Val Lys
              12245   12250   12255
Lys Thr Ser Phe His Val Thr Asn Leu Val Pro Gly Asn Glu Tyr Tyr
              12260   12265   12270
Phe Arg Val Thr Ala Val Asn Glu Tyr Gly Pro Gly Val Pro Thr Asp
          12275   12280   12285
Val Pro Lys Pro Val Leu Ala Ser Asp Pro Leu Ser Glu Pro Asp Pro
    12290   12295   12300   1
Pro Arg Lys Leu Glu Ala Thr Glu Met Thr Lys Asn Ser Ala Thr Leu
2305   12310   12315   12320
Ala Trp Leu Pro Pro Leu Arg Asp Gly Gly Ala Lys Ile Asp Gly Tyr
              12325   12330   12335
Ile Ile Ser Tyr Arg Glu Glu Glu Gln Pro Ala Asp Arg Trp Thr Glu
          12340   12345   12350
Tyr Ser Val Val Lys Asp Leu Ser Leu Val Val Thr Gly Leu Lys Glu
    12355   12360   12365
Gly Lys Lys Tyr Lys Phe Arg Val Ala Ala Arg Asn Ala Val Gly Val
    12370   12375   12380   1
Ser Leu Pro Arg Glu Ala Glu Gly Val Tyr Glu Ala Lys Glu Gln Leu
2385   12390   12395   12400
Leu Pro Pro Lys Ile Leu Met Pro Glu Gln Ile Thr Ile Lys Ala Gly
              12405   12410   12415
Lys Lys Leu Arg Ile Glu Ala His Val Tyr Gly Lys Pro His Pro Thr
          12420   12425   12430
Cys Lys Trp Lys Lys Gly Glu Asp Glu Val Val Thr Ser Ser His Leu
          12435   12440   12445
Ala Val His Lys Ala Asp Ser Ser Ser Ile Leu Ile Ile Lys Asp Val
    12450   12455   12460   1
Thr Arg Lys Asp Ser Gly Tyr Tyr Ser Leu Thr Ala Glu Asn Ser Ser
2465   12470   12475   12480
Gly Thr Asp Thr Gln Lys Ile Lys Val Val Val Met Asp Ala Pro Gly
              12485   12490   12495
Pro Pro Gln Pro Pro Phe Asp Ile Ser Asp Ile Asp Ala Asp Ala Cys
              12500   12505   12510
Ser Leu Ser Trp His Ile Pro Leu Glu Asp Gly Gly Ser Asn Ile Thr
          12515   12520   12525
Asn Tyr Ile Val Glu Lys Cys Asp Val Ser Arg Gly Asp Trp Val Thr
    12530   12535   12540   1
Ala Leu Ala Ser Val Thr Lys Thr Ser Cys Arg Val Gly Lys Leu Ile
2545   12550   12555   12560
Pro Gly Gln Glu Tyr Ile Phe Arg Val Arg Ala Glu Asn Arg Phe Gly
              12565   12570   12575
Ile Ser Glu Pro Leu Thr Ser Pro Lys Met Val Ala Gln Phe Pro Phe
          12580   12585   12590
Gly Val Pro Ser Glu Pro Lys Asn Ala Arg Val Thr Lys Val Asn Lys
          12595   12600   12605
Asp Cys Ile Phe Val Ala Trp Asp Arg Pro Asp Ser Asp Gly Gly Ser
    12610   12615   12620   1

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Pro Ile Ile Gly Tyr Leu Ile Glu Arg Lys Glu Arg Asn Ser Leu Leu
2625             12630                 12635                 12640
Trp Val Lys Ala Asn Asp Thr Leu Val Arg Ser Thr Glu Tyr Pro Cys
            12645                 12650                 12655
Ala Gly Leu Val Glu Gly Leu Glu Tyr Ser Phe Arg Ile Tyr Ala Leu
            12660                 12665                 12670
Asn Lys Ala Gly Ser Ser Pro Pro Ser Lys Pro Thr Glu Tyr Val Thr
    12675                 12680                 12685
Ala Arg Met Pro Val Asp Pro Pro Gly Lys Pro Glu Val Ile Asp Val
    12690                 12695                 12700             1
Thr Lys Ser Thr Val Ser Leu Ile Trp Ala Arg Pro Lys His Asp Gly
2705                 12710                 12715                 12720
Gly Ser Lys Ile Ile Gly Tyr Phe Val Glu Ala Cys Lys Leu Pro Gly
            12725                 12730                 12735
Asp Lys Trp Val Arg Cys Asn Thr Ala Pro His Gln Ile Pro Gln Glu
            12740                 12745                 12750
Glu Tyr Thr Ala Thr Gly Leu Glu Glu Lys Ala Gln Tyr Gln Phe Arg
    12755                 12760                 12765
Ala Ile Ala Arg Thr Ala Val Asn Ile Ser Pro Pro Ser Glu Pro Ser
    12770                 12775                 12780             1
Asp Pro Val Thr Ile Leu Ala Glu Asn Val Pro Pro Arg Ile Asp Leu
2785                 12790                 12795                 12800
Ser Val Ala Met Lys Ser Leu Leu Thr Val Lys Ala Gly Thr Asn Val
            12805                 12810                 12815
Cys Leu Asp Ala Thr Val Phe Gly Lys Pro Met Pro Thr Val Ser Trp
    12820                 12825                 12830
Lys Lys Asp Gly Thr Leu Leu Lys Pro Ala Glu Gly Ile Lys Met Ala
    12835                 12840                 12845
Met Gln Arg Asn Leu Cys Thr Leu Glu Leu Phe Ser Val Asn Arg Lys
    12850                 12855                 12860             1
Asp Ser Gly Asp Tyr Thr Ile Thr Ala Glu Asn Ser Ser Gly Ser Lys
2865                 12870                 12875                 12880
Ser Ala Thr Ile Lys Leu Lys Val Leu Asp Lys Pro Gly Pro Pro Ala
            12885                 12890                 12895
Ser Val Lys Ile Asn Lys Met Tyr Ser Asp Arg Ala Met Leu Ser Trp
    12900                 12905                 12910
Glu Pro Pro Leu Glu Asp Gly Gly Ser Glu Ile Thr Asn Tyr Ile Val
    12915                 12920                 12925
Asp Lys Arg Glu Thr Ser Arg Pro Asn Trp Ala Gln Val Ser Ala Thr
    12930                 12935                 12940             1
Val Pro Ile Thr Ser Cys Ser Val Glu Lys Leu Ile Glu Gly His Glu
2945                 12950                 12955                 12960
Tyr Gln Phe Arg Ile Cys Ala Glu Asn Lys Tyr Gly Val Gly Asp Pro
            12965                 12970                 12975
Val Phe Thr Glu Pro Ala Ile Ala Lys Asn Pro Tyr Asp Pro Pro Gly
            12980                 12985                 12990
Arg Cys Asp Pro Pro Val Ile Ser Asn Ile Thr Lys Asp His Met Thr
    12995                 13000                 13005
Val Ser Trp Lys Pro Pro Ala Asp Asp Gly Gly Ser Pro Ile Thr Gly
    13010                 13015                 13020             1
Tyr Leu Leu Glu Lys Arg Glu Thr Gln Ala Val Asn Trp Thr Lys Val
3025             13030                 13035                 13040
Asn Arg Lys Pro Ile Ile Glu Arg Thr Leu Lys Ala Thr Gly Leu Gln
            13045                 13050                 13055
Glu Gly Thr Glu Tyr Glu Phe Arg Val Thr Ala Ile Asn Lys Ala Gly
            13060                 13065                 13070
Pro Gly Lys Pro Ser Asp Ala Ser Lys Ala Ala Tyr Ala Arg Asp Pro
    13075                 13080                 13085
Gln Tyr Pro Pro Ala Pro Pro Ala Phe Pro Lys Val Tyr Asp Thr Thr
    13090                 13095                 13100             1
Arg Ser Ser Val Ser Leu Ser Trp Gly Lys Pro Ala Tyr Asp Gly Gly
3105                 13110                 13115                 13120
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Ser Pro Ile Ile Gly Tyr Leu Val Glu Val Lys Arg Ala Asp Ser Asp
        13125              13130                  13135
Asn Trp Val Arg Cys Asn Leu Pro Gln Asn Leu Gln Lys Thr Arg Phe
        13140              13145              13150
Glu Val Thr Gly Leu Met Glu Asp Thr Gln Tyr Gln Phe Arg Val Tyr
        13155              13160              13165
Ala Val Asn Lys Ile Gly Tyr Ser Asp Pro Ser Asp Val Pro Asp Lys
   13170              13175              13180                  1
His Tyr Pro Lys Asp Ile Leu Ile Pro Pro Glu Gly Glu His Asp Ala
3185              13190              13195              13200
Asp Leu Arg Lys Thr Leu Ile Leu Arg Ala Gly Val Thr Met Arg Leu
        13205              13210              13215
Tyr Val Pro Val Lys Gly Arg Pro Pro Pro Lys Ile Thr Trp Ser Lys
        13220              13225              13230
Pro Asn Val Asn Leu Arg Asp Arg Ile Gly Leu Asp Ile Lys Ser Thr
        13235              13240              13245
Asp Phe Asp Thr Phe Leu Arg Cys Glu Asn Val Asn Lys Tyr Asp Ala
   13250              13255              13260                  1
Gly Lys Tyr Ile Leu Thr Leu Glu Asn Ser Cys Gly Lys Lys Glu Tyr
3265              13270              13275              13280
Thr Ile Val Val Lys Val Leu Asp Thr Pro Gly Pro Pro Ile Asn Val
        13285              13290              13295
Thr Val Lys Glu Ile Ser Lys Asp Ser Ala Tyr Val Thr Trp Glu Pro
        13300              13305              13310
Pro Ile Ile Asp Gly Gly Ser Pro Ile Ile Asn Tyr Val Val Gln Lys
        13315              13320              13325
Arg Asp Ala Glu Arg Lys Ser Trp Ser Thr Val Thr Thr Glu Cys Ser
   13330              13335              13340                  1
Lys Thr Ser Phe Arg Val Pro Asn Leu Glu Glu Gly Lys Ser Tyr Phe
3345              13350              13355              13360
Phe Arg Val Phe Ala Glu Asn Glu Tyr Gly Ile Gly Asp Pro Gly Glu
        13365              13370              13375
Thr Arg Asp Ala Val Lys Ala Ser Gln Thr Pro Gly Pro Val Val Asp
        13380              13385              13390
Leu Lys Val Arg Ser Val Ser Lys Ser Ser Cys Ser Ile Gly Trp Lys
        13395              13400              13405
Lys Pro His Ser Asp Gly Gly Ser Arg Ile Ile Gly Tyr Val Val Asp
   13410              13415              13420                  1
Phe Leu Thr Glu Glu Asn Lys Trp Gln Arg Val Met Lys Ser Leu Ser
3425              13430              13435              13440
Leu Gln Tyr Ser Ala Lys Asp Leu Thr Glu Gly Lys Glu Tyr Thr Phe
        13445              13450              13455
Arg Val Ser Ala Glu Asn Glu Asn Gly Glu Gly Thr Pro Ser Glu Ile
        13460              13465              13470
Thr Val Val Ala Arg Asp Asp Val Val Ala Pro Asp Leu Asp Leu Lys
        13475              13480              13485
Gly Leu Pro Asp Leu Cys Tyr Leu Ala Lys Glu Asn Ser Asn Phe Arg
   13490              13495              13500                  1
Leu Lys Ile Pro Ile Lys Gly Lys Pro Ala Pro Ser Val Ser Trp Lys
3505              13510              13515              13520
Lys Gly Glu Asp Pro Leu Ala Thr Asp Thr Arg Val Ser Val Glu Ser
        13525              13530              13535
Ser Ala Val Asn Thr Thr Leu Ile Val Tyr Asp Cys Gln Lys Ser Asp
        13540              13545              13550
Ala Gly Lys Tyr Thr Ile Thr Leu Lys Asn Val Ala Gly Thr Lys Glu
        13555              13560              13565
Gly Thr Ile Ser Ile Lys Val Val Gly Lys Pro Gly Ile Pro Thr Gly
   13570              13575              13580                  1
Pro Ile Lys Phe Asp Glu Val Thr Ala Glu Ala Met Thr Leu Lys Trp
3585              13590              13595              13600
Ala Pro Pro Lys Asp Asp Gly Gly Ser Glu Ile Thr Asn Tyr Ile Leu
        13605              13610              13615
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Glu Lys Arg Asp Ser Val Asn Asn Lys Trp Val Thr Cys Ala Ser Ala
　　　13620　　　　　　　　　13625　　　　　　　　　13630
Val Gln Lys Thr Thr Phe Arg Val Thr Arg Leu His Glu Gly Met Glu
　　　13635　　　　　　　　　13640　　　　　　　　　13645
Tyr Thr Phe Arg Val Ser Ala Glu Asn Lys Tyr Gly Val Gly Glu Gly
　　13650　　　　　　　　　13655　　　　　　　　　13660　　　　1
Leu Lys Ser Glu Pro Ile Val Ala Arg His Pro Phe Asp Val Pro Asp
3665　　　　　　　　13670　　　　　　　　13675　　　　　　　　13680
Ala Pro Pro Pro Asn Ile Val Asp Val Arg His Asp Ser Val Ser
　　　13685　　　　　　　　　13690　　　　　　　　　13695
Leu Thr Trp Thr Asp Pro Lys Lys Thr Gly Gly Ser Pro Ile Thr Gly
　　　13700　　　　　　　　　13705　　　　　　　　　13710
Tyr His Leu Glu Phe Lys Glu Arg Asn Ser Leu Leu Trp Lys Arg Ala
　　　13715　　　　　　　　　13720　　　　　　　　　13725
Asn Lys Thr Pro Ile Arg Met Arg Asp Phe Lys Val Thr Gly Leu Thr
　　13730　　　　　　　　　13735　　　　　　　　　13740　　　　1
Glu Gly Leu Glu Tyr Glu Phe Arg Val Met Ala Ile Asn Leu Ala Gly
3745　　　　　　　　13750　　　　　　　　13755　　　　　　　　13760
Val Gly Lys Pro Ser Leu Pro Ser Glu Pro Val Val Ala Leu Asp Pro
　　　　　13765　　　　　　　　　13770　　　　　　　　　13775
Ile Asp Pro Pro Gly Lys Pro Glu Val Ile Asn Ile Thr Arg Asn Ser
　　　13780　　　　　　　　　13785　　　　　　　　　13790
Val Thr Leu Ile Trp Thr Glu Pro Lys Tyr Asp Gly Gly His Lys Leu
　　　13795　　　　　　　　　13800　　　　　　　　　13805
Thr Gly Tyr Ile Val Glu Lys Arg Asp Leu Pro Ser Lys Ser Trp Met
　　13810　　　　　　　　　13815　　　　　　　　　13820　　　　1
Lys Ala Asn His Val Asn Val Pro Glu Cys Ala Phe Thr Val Thr Asp
3825　　　　　　　　13830　　　　　　　　13835　　　　　　　　13840
Leu Val Glu Gly Gly Lys Tyr Glu Phe Arg Ile Arg Ala Lys Asn Thr
　　　　　13845　　　　　　　　　13850　　　　　　　　　13855
Ala Gly Ala Ile Ser Ala Pro Ser Glu Ser Thr Glu Thr Ile Ile Cys
　　　13860　　　　　　　　　13865　　　　　　　　　13870
Lys Asp Glu Tyr Glu Ala Pro Thr Ile Val Leu Asp Pro Thr Ile Lys
　　　13875　　　　　　　　　13880　　　　　　　　　13885
Asp Gly Leu Thr Ile Lys Ala Gly Asp Thr Ile Val Leu Asn Ala Ile
　　13890　　　　　　　　　13895　　　　　　　13900　　　　　　1
Ser Ile Leu Gly Lys Pro Leu Pro Lys Ser Ser Trp Ser Lys Ala Gly
3905　　　　　　　　13910　　　　　　　　13915　　　　　　　　13920
Lys Asp Ile Arg Pro Ser Asp Ile Thr Gln Ile Thr Ser Thr Pro Thr
　　　　　13925　　　　　　　　　13930　　　　　　　　　13935
Ser Ser Met Leu Thr Ile Lys Tyr Ala Thr Arg Lys Asp Ala Gly Glu
　　　13940　　　　　　　　　13945　　　　　　　　　13950
Tyr Thr Ile Thr Ala Thr Asn Pro Phe Gly Thr Lys Val Glu His Val
　　　13955　　　　　　　　　13960　　　　　　　　　13965
Lys Val Thr Val Leu Asp Val Pro Gly Pro Pro Gly Pro Val Glu Ile
　　　13970　　　　　　　　　13975　　　　　　　　　13980　　　　1
Ser Asn Val Ser Ala Glu Lys Ala Thr Leu Thr Trp Thr Pro Pro Leu
3985　　　.　　　　　13990　　　　　　　　13995　　　　　　　　14000
Glu Asp Gly Gly Ser Pro Ile Lys Ser Tyr Ile Leu Glu Lys Arg Glu
　　　　　14005　　　　　　　　　14010　　　　　　　　　14015
Thr Ser Arg Leu Leu Trp Thr Val Val Ser Glu Asp Ile Gln Ser Cys
　　　14020　　　　　　　　　14025　　　　　　　　　14030
Arg His Val Ala Thr Lys Leu Ile Gln Gly Asn Glu Tyr Ile Phe Arg
　　　14035　　　　　　　　　14040　　　　　　　　　14045
Val Ser Ala Val Asn His Tyr Gly Lys Gly Glu Pro Val Gln Ser Glu
　　14050　　　　　　　　　14055　　　　　　　　　14060　　　　1
Pro Val Lys Met Val Asp Arg Phe Gly Pro Pro Gly Pro Pro Glu Lys
4065　　　　　　　　14070　　　　　　　　14075　　　　　　　　14080
Pro Glu Val Ser Asn Val Thr Lys Asn Thr Ala Thr Val Ser Trp Lys
　　　　　14085　　　　　　　　　14090　　　　　　　　　14095
Arg Pro Val Asp Asp Gly Gly Ser Glu Ile Thr Gly Tyr His Val Glu
　　　14100　　　　　　　　　14105　　　　　　　　　14110

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Arg Arg Glu Lys Lys Ser Leu Arg Trp Val Arg Ala Ile Lys Thr Pro
    14115                   14120                   14125
Val Ser Asp Leu Arg Cys Lys Val Thr Gly Leu Gln Glu Gly Ser Thr
    14130               14135               14140                1
Tyr Glu Phe Arg Val Ser Ala Glu Asn Arg Ala Gly Ile Gly Pro Pro
4145                14150               14155               14160
Ser Glu Ala Ser Asp Ser Val Leu Met Lys Asp Ala Ala Tyr Pro Pro
                14165               14170               14175
Gly Pro Pro Ser Asn Pro His Val Thr Asp Thr Thr Lys Lys Ser Ala
            14180               14185               14190
Ser Leu Ala Trp Gly Lys Pro His Tyr Asp Gly Gly Leu Glu Ile Thr
        14195               14200               14205
Gly Tyr Val Val Glu His Gln Lys Val Gly Asp Glu Ala Trp Ile Lys
    14210               14215               14220                1
Asp Thr Thr Gly Thr Ala Leu Arg Ile Thr Gln Phe Val Val Pro Asp
4225                14230               14235               14240
Leu Gln Thr Lys Glu Lys Tyr Asn Phe Arg Ile Ser Ala Ile Asn Asp
        14245               14250                14255
Ala Gly Val Gly Glu Pro Ala Val Ile Pro Asp Val Glu Ile Val Glu
            14260               14265               14270
Arg Glu Met Ala Pro Asp Phe Glu Leu Asp Ala Glu Leu Arg Arg Thr
        14275               14280               14285
Leu Val Val Arg Ala Gly Leu Ser Ile Arg Ile Phe Val Pro Ile Lys
    14290               14295               14300                1
Gly Arg Pro Ala Pro Glu Val Thr Trp Thr Lys Asp Asn Ile Asn Leu
4305                14310               14315               14320
Lys Asn Arg Ala Asn Ile Glu Asn Thr Glu Ser Phe Thr Leu Leu Ile
            14325               14330               14335
Ile Pro Glu Cys Asn Arg Tyr Asp Thr Gly Lys Phe Val Met Thr Ile
        14340               14345               14350
Glu Asn Pro Ala Gly Lys Lys Ser Gly Phe Val Asn Val Arg Val Leu
        14355               14360               14365
Asp Thr Pro Gly Pro Val Leu Asn Leu Arg Pro Thr Asp Ile Thr Lys
    14370               14375               14380                1
Asp Ser Val Thr Leu His Trp Asp Leu Pro Leu Ile Asp Gly Gly Ser
4385                14390               14395               14400
Arg Ile Thr Asn Tyr Ile Val Glu Lys Arg Glu Ala Thr Arg Lys Ser
            14405               14410               14415
Tyr Ser Thr Ala Thr Thr Lys Cys His Lys Cys Thr Tyr Lys Val Thr
        14420               14425               14430
Gly Leu Ser Glu Gly Cys Glu Tyr Phe Phe Arg Val Met Ala Glu Asn
    14435               14440               14445
Glu Tyr Gly Ile Gly Glu Pro Thr Glu Thr Thr Glu Pro Val Lys Ala
    14450               14455               14460                1
Ser Glu Ala Pro Ser Pro Pro Asp Ser Leu Asn Ile Met Asp Ile Thr
4465                14470               14475               14480
Lys Ser Thr Val Ser Leu Ala Trp Pro Lys Pro Lys His Asp Gly Gly
            14485               14490               14495
Ser Lys Ile Thr Gly Tyr Val Ile Glu Ala Gln Arg Lys Gly Ser Asp
        14500               14505               14510
Gln Trp Thr His Ile Thr Thr Val Lys Gly Leu Glu Cys Val Val Arg
    14515               14520               14525
Asn Leu Thr Glu Gly Glu Glu Tyr Thr Phe Gln Val Met Ala Val Asn
    14530               14535               14540                1
Ser Ala Gly Arg Ser Ala Pro Arg Glu Ser Arg Pro Val Ile Val Lys
4545                14550               14555               14560
Glu Gln Thr Met Leu Pro Glu Leu Asp Leu Arg Gly Ile Tyr Gln Lys
            14565               14570               14575
Leu Val Ile Ala Lys Ala Gly Asp Asn Ile Lys Val Glu Ile Pro Val
        14580               14585               14590
Leu Gly Arg Pro Lys Pro Thr Val Thr Trp Lys Lys Gly Asp Gln Ile
        14595               14600               14605
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Leu Lys Gln Thr Gln Arg Val Asn Phe Glu Thr Thr Ala Thr Ser Thr
    14610           14615           14620                    1
Ile Leu Asn Ile Asn Glu Cys Val Arg Ser Asp Ser Gly Pro Tyr Pro
4625            14630           14635                    14640
Leu Thr Ala Arg Asn Ile Val Gly Glu Val Gly Asp Val Ile Thr Ile
            14645           14650           14655
Gln Val His Asp Ile Pro Gly Pro Pro Thr Gly Pro Ile Lys Phe Asp
        14660           14665           14670
Glu Val Ser Ser Asp Phe Val Thr Phe Ser Trp Asp Pro Pro Glu Asn
    14675           14680           14685
Asp Gly Gly Val Pro Ile Ser Asn Tyr Val Val Glu Met Arg Gln Thr
    14690           14695           14700                    1
Asp Ser Thr Thr Trp Val Glu Leu Ala Thr Thr Val Ile Arg Thr Thr
4705            14710           14715                    14720
Tyr Lys Ala Thr Arg Leu Thr Thr Gly Leu Glu Tyr Gln Phe Arg Val
            14725           14730           14735
Lys Ala Gln Asn Arg Tyr Gly Val Gly Pro Gly Ile Thr Ser Ala Trp
    14740           14745           14750
Ile Val Ala Asn Tyr Pro Phe Lys Val Pro Gly Pro Pro Gly Thr Pro
    14755           14760           14765
Gln Val Thr Ala Val Thr Lys Asp Ser Met Thr Ile Ser Trp His Glu
    14770           14775           14780                    1
Pro Leu Ser Asp Gly Gly Ser Pro Ile Leu Gly Tyr His Val Glu Arg
4785            14790           14795                    14800
Lys Glu Arg Asn Gly Ile Leu Trp Gln Thr Val Ser Lys Ala Leu Val
            14805           14810           14815
Pro Gly Asn Ile Phe Lys Ser Ser Gly Leu Thr Asp Gly Ile Ala Tyr
    14820           14825           14830
Glu Phe Arg Val Ile Ala Glu Asn Met Ala Gly Lys Ser Lys Pro Ser
        14835           14840           14845 ·
Lys Pro Ser Glu Pro Met Leu Ala Leu Asp Pro Ile Asp Pro Pro Gly
    14850           14855           14860                    1
Lys Pro Val Pro Leu Asn Ile Thr Arg His Thr Val Thr Leu Lys Trp
4865            14870           14875                    14880
Ala Lys Pro Glu Tyr Thr Gly Gly Phe Lys Ile Thr Ser Tyr Ile Val
            14885           14890           14895
Glu Lys Arg Asp Leu Pro Asn Gly Arg Trp Leu Lys Ala Asn Phe Ser
        14900           14905           14910
Asn Ile Leu Glu Asn Glu Phe Thr Val Ser Gly Leu Thr Glu Asp Ala
    14915           14920           14925
Ala Tyr Glu Phe Arg Val Ile Ala Lys Asn Ala Ala Gly Ala Ile Ser
    14930           14935           14940                    1
Pro Pro Ser Glu Pro Ser Asp Ala Ile Thr Cys Arg Asp Asp Val Glu
4945            14950           14955                    14960
Ala Pro Lys Ile Lys Val Asp Val Lys Phe Lys Asp Thr Val Ile Leu
            14965           14970           14975
Lys Ala Gly Glu Ala Phe Arg Leu Glu Ala Asp Val Ser Gly Arg Pro
        14980           14985           14990
Pro Pro Thr Met Glu Trp Ser Lys Asp Gly Lys Glu Leu Glu Gly Thr
        14995           15000           15005
Ala Lys Leu Glu Ile Lys Ile Ala Asp Phe Ser Thr Asn Leu Val Asn
    15010           15015           15020                    1
Lys Asp Ser Thr Arg Arg Asp Ser Gly Ala Tyr Thr Leu Thr Ala Thr
5025            15030           15035                    15040
Asn Pro Gly Gly Phe Ala Lys His Ile Phe Asn Val Lys Val Leu Asp
            15045           15050           15055
Arg Pro Gly Pro Pro Glu Gly Pro Leu Ala Val Thr Glu Val Thr Ser
        15060           15065           15070
Glu Lys Cys Val Leu Ser Trp Phe Pro Pro Leu Asp Asp Gly Gly Ala
        15075           15080           15085
Lys Ile Asp His Tyr Ile Val Gln Lys Arg Glu Thr Ser Arg Leu Ala
    15090           15095           15100                    1
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Trp Thr Asn Val Ala Ser Glu Val Gln Val Thr Lys Leu Lys Val Thr
5105             15110             15115             15120
Lys Leu Leu Lys Gly Asn Glu Tyr Ile Phe Arg Val Met Ala Val Asn
        15125             15130             15135
Lys Tyr Gly Val Gly Glu Pro Leu Glu Ser Glu Pro Val Leu Ala Val
        15140             15145             15150
Asn Pro Tyr Gly Pro Pro Asp Pro Pro Lys Asn Pro Glu Val Thr Thr
        15155             15160             15165
Ile Thr Lys Asp Ser Met Val Val Cys Trp Gly His Pro Asp Ser Asp
        15170             15175             15180             1
Gly Gly Ser Glu Ile Ile Asn Tyr Ile Val Glu Arg Arg Asp Lys Ala
5185             15190             15195             15200
Gly Gln Arg Trp Ile Lys Cys Asn Lys Lys Thr Leu Thr Asp Leu Arg
        15205             15210             15215
Tyr Lys Val Ser Gly Leu Thr Glu Gly His Glu Tyr Glu Phe Arg Ile
        15220             15225             15230
Met Ala Glu Asn Ala Ala Gly Ile Ser Ala Pro Ser Pro Thr Ser Pro
        15235             15240             15245
Phe Tyr Lys Ala Cys Asp Thr Val Phe Lys Pro Gly Pro Pro Gly Asn
        15250             15255             15260             1
Pro Arg Val Leu Asp Thr Ser Arg Ser Ser Ile Ser Ile Ala Trp Asn
5265             15270             15275             15280
Lys Pro Ile Tyr Asp Gly Gly Ser Glu Ile Thr Gly Tyr Met Val Glu
        15285             15290             15295
Ile Ala Leu Pro Glu Glu Asp Glu Trp Gln Ile Val Thr Pro Pro Ala
        15300             15305             15310
Gly Leu Lys Ala Thr Ser Tyr Thr Ile Thr Gly Leu Thr Glu Asn Gln
        15315             15320             15325
Glu Tyr Lys Ile Arg Ile Tyr Ala Met Asn Ser Glu Gly Leu Gly Glu
        15330             15335             15340             1
Pro Ala Leu Val Pro Gly Thr Pro Lys Ala Glu Asp Arg Met Leu Pro
5345             15350             15355             15360
Pro Glu Ile Glu Leu Asp Ala Asp Leu Arg Lys Val Val Thr Ile Arg
        15365             15370             15375
Ala Cys Cys Thr Leu Arg Leu Phe Val Pro Ile Lys Gly Arg Pro Asp
        15380             15385             .15390
Pro Glu Val Lys Trp Ala Arg Asp His Gly Glu Ser Leu Asp Lys Ala
        15395             15400             15405
Ser Ile Glu Ser Ala Ser Ser Tyr Thr Leu Leu Ile Val Gly Asn Val
        15410             15415             15420             1
Asn Arg Phe Asp Ser Gly Lys Tyr Ile Leu Thr Val Glu Asn Ser Ser
5425             15430             15435             15440
Gly Ser Lys Ser Ala Phe Val Asn Val Arg Val Leu Asp Thr Pro Gly
        15445             15450             15455
Pro Pro Gln Asp Leu Lys Val Lys Glu Val Thr Lys Thr Ser Val Thr
        15460             15465             15470
Leu Thr Trp Asp Pro Pro Leu Leu Asp Gly Gly Ser Lys Ile Lys Asn
        15475             15480             15485
Tyr Ile Val Glu Lys Arg Glu Ser Thr Arg Lys Ala Tyr Ser Thr Val
        15490             15495             15500             1
Ala Thr Asn Cys His Lys Thr Ser Trp Lys Val Asp Gln Leu Gln Glu
5505             15510             15515             15520
Gly Cys Ser Tyr Tyr Phe Arg Val Leu Ala Glu Asn Glu Tyr Gly Ile
        15525             15530             15535
Gly Leu Pro Ala Glu Thr Ala Glu Ser Val Lys Ala Ser Glu Arg Pro
        15540             15545             15550
Leu Pro Pro Gly Lys Ile Thr Leu Met Asp Val Thr Arg Asn Ser Val
        15555             15560             15565
Ser Leu Ser Trp Glu Lys Pro Glu His Asp Gly Gly Ser Arg Ile Leu
        15570             15575             15580             1
Gly Tyr Ile Val Glu Met Gln Thr Lys Gly Ser Asp Lys Trp Ala Thr
5585             15590             15595             15600
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Cys Ala Thr Val Lys Val Thr Glu Ala Thr Ile Thr Gly Leu Ile Gln
            15605               15610               15615
Gly Glu Glu Tyr Ser Phe Arg Val Ser Ala Gln Asn Glu Lys Gly Ile
            15620               15625               15630
Ser Asp Pro Arg Gln Leu Ser Val Pro Val Ile Ala Lys Asp Leu Val
            15635               15640               15645
Ile Pro Pro Ala Phe Lys Leu Leu Phe Asn Thr Phe Thr Val Leu Ala
        15650               15655               15660              1
Gly Glu Asp Leu Lys Val Asp Val Pro Phe Ile Gly Arg Pro Thr Pro
    5665               15670               15675               15680
Ala Val Thr Trp His Lys Asp Asn Val Pro Leu Lys Gln Thr Thr Arg
            15685               15690               15695
Val Asn Ala Glu Ser Thr Glu Asn Asn Ser Leu Leu Thr Ile Lys Asp
            15700               15705               15710
Ala Cys Arg Glu Asp Val Gly His Tyr Val Val Lys Leu Thr Asn Ser
        15715               15720               15725
Ala Gly Glu Ala Ile Glu Thr Leu Asn Val Ile Val Leu Asp Lys Pro
        15730               15735               15740              1
Gly Pro Pro Thr Gly Pro Val Lys Met Asp Glu Val Thr Ala Asp Ser
    5745               15750               15755               15760
Ile Thr Leu Ser Trp Gly Pro Pro Lys Tyr Asp Gly Gly Ser Ser Ile
            15765               15770               15775
Asn Asn Tyr Ile Val Glu Lys Arg Asp Thr Ser Thr Thr Thr Trp Gln
            15780               15785               15790
Ile Val Ser Ala Thr Val Ala Arg Thr Thr Ile Lys Ala Cys Arg Leu
        15795               15800               15805
Lys Thr Gly Cys Glu Tyr Gln Phe Arg Ile Ala Ala Glu Asn Arg Tyr
    15810               15815               15820              1
Gly Lys Ser Thr Tyr Leu Asn Ser Glu Pro Thr Val Ala Gln Tyr Pro
    5825               15830               15835               15840
Phe Lys Val Pro Gly Pro Pro Gly Thr Pro Val Val Thr Leu Ser Ser
            15845               15850               15855
Arg Asp Ser Met Glu Val Gln Trp Asn Glu Pro Ile Ser Asp Gly Gly
            15860               15865               15870
Ser Arg Val Ile Gly Tyr His Leu Glu Arg Lys Glu Arg Asn Ser Ile
        15875               15880               15885
Leu Trp Val Lys Leu Asn Lys Thr Pro Ile Pro Gln Thr Lys Phe Lys
    15890               15895               15900              1
Thr Thr Gly Leu Glu Glu Gly Val Glu Tyr Glu Phe Arg Val Ser Ala
    5905               15910               15915               15920
Glu Asn Ile Val Gly Ile Gly Lys Pro Ser Lys Val Ser Glu Cys Tyr
            15925               15930               15935
Val Ala Arg Asp Pro Cys Asp Pro Pro Gly Arg Pro Glu Ala Ile Ile
            15940               15945               15950
Val Thr Arg Asn Ser Val Thr Leu Gln Trp Lys Lys Pro Thr Tyr Asp
        15955               15960               15965
Gly Gly Ser Lys Ile Thr Gly Tyr Ile Val Glu Lys Lys Glu Leu Pro
    15970               15975               15980              1
Glu Gly Arg Trp Met Lys Ala Ser Phe Thr Asn Ile Ile Asp Thr His
    5985               15990               15995               16000
Phe Glu Val Thr Gly Leu Val Glu Asp His Arg Tyr Glu Phe Arg Val
            16005               16010               16015
Ile Ala Arg Asn Ala Ala Gly Val Phe Ser Glu Pro Ser Glu Ser Thr
            16020               16025               16030
Gly Ala Ile Thr Ala Arg Asp Glu Val Asp Pro Pro Arg Ile Ser Met
        16035               16040               16045
Asp Pro Lys Tyr Lys Asp Thr Ile Val Val His Ala Gly Glu Ser Phe
    16050               16055               16060              1
Lys Val Asp Ala Asp Ile Tyr Gly Lys Pro Ile Pro Thr Ile Gln Trp
    6065               16070               16075               16080
Ile Lys Gly Asp Gln Glu Leu Ser Asn Thr Ala Arg Leu Glu Ile Lys
            16085               16090               16095
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Ser Thr Asp Phe Ala Thr Ser Leu Ser Val Lys Asp Ala Val Arg Val
          16100                 16105                 16110
Asp Ser Gly Asn Tyr Ile Leu Lys Ala Lys Asn Val Ala Gly Glu Arg
          16115                 16120                 16125
Ser Val Thr Val Asn Val Lys Val Leu Asp Arg Pro Gly Pro Pro Glu
        16130                 16135                 16140           1
Gly Pro Val Val Ile Ser Gly Val Thr Ala Glu Lys Cys Thr Leu Ala
6145               16150                 16155                 16160
Trp Lys Pro Pro Leu Gln Asp Gly Gly Ser Asp Ile Ile Asn Tyr Ile
          16165                 16170                 16175
Val Glu Arg Arg Glu Thr Ser Arg Leu Val Trp Thr Val Val Asp Ala
          16180                 16185                 16190
Asn Val Gln Thr Leu Ser Cys Lys Val Thr Lys Leu Leu Glu Gly Asn
        16195                 16200                 16205
Glu Tyr Thr Phe Arg Ile Met Ala Val Asn Lys Tyr Gly Val Gly Glu
        16210                 16215                 16220           1
Pro Leu Glu Ser Glu Pro Val Val Ala Lys Asn Pro Phe Val Val Pro
6225               16230                 16235                 16240
Asp Ala Pro Lys Ala Pro Glu Val Thr Thr Val Thr Lys Asp Ser Met
          16245                 16250                 16255
Ile Val Val Trp Glu Arg Pro Ala Ser Asp Gly Gly Ser Glu Ile Leu
          16260                 16265                 16270
Gly Tyr Val Leu Glu Lys Arg Asp Lys Glu Gly Ile Arg Trp Thr Arg
        16275                 16280                 16285
Cys His Lys Arg Leu Ile Gly Glu Leu Arg Leu Arg Val Thr Gly Leu
        16290                 16295                 16300           1
Ile Glu Asn His Asp Tyr Glu Phe Arg Val Ser Ala Glu Asn Ala Ala
6305               16310                 16315                 16320
Gly Leu Ser Glu Pro Ser Pro Pro Ser Ala Tyr Gln Lys Ala Cys Asp
          16325                 16330                 16335
Pro Ile Tyr Lys Pro Gly Pro Pro Asn Asn Pro Lys Val Ile Asp Ile
        16340                 16345                 16350
Thr Arg Ser Ser Val Phe Leu Ser Trp Ser Lys Pro Ile Tyr Asp Gly
        16355                 16360                 16365
Gly Cys Glu Ile Gln Gly Tyr Ile Val Glu Lys Cys Asp Val Asn Val
        16370                 16375                 16380           1
Gly Glu Trp Thr Met Cys Thr Pro Pro Thr Gly Ile Asn Lys Thr Asn
6385               16390                 16395                 16400
Ile Glu Val Glu Lys Leu Leu Glu Lys His Glu Tyr Asn Phe Arg Ile
          16405                 16410                 16415
Cys Ala Ile Asn Lys Ala Gly Val Gly Glu His Ala Asp Val Pro Gly
        16420                 16425                 16430
Pro Ile Ile Val Glu Glu Lys Leu Glu Ala Pro Asp Ile Asp Leu Asp
        16435                 16440                 16445
Leu Glu Leu Arg Lys Ile Ile Asn Ile Arg Ala Gly Gly Ser Leu Arg
        16450                 16455                 16460           1
Leu Phe Val Pro Ile Lys Gly Arg Pro Thr Pro Glu Val Lys Trp Gly
6465               16470                 16475                 16480
Lys Val Asp Gly Glu Ile Arg Asp Ala Ala Ile Ile Asp Val Thr Ser
          16485                 16490                 16495
Ser Phe Thr Ser Leu Val Leu Asp Asn Val Asn Arg Tyr Asp Ser Gly
        16500                 16505                 16510
Lys Tyr Thr Leu Thr Leu Glu Asn Ser Ser Gly Thr Lys Ser Ala Phe
        16515                 16520                 16525
Val Thr Val Arg Val Leu Asp Thr Pro Ser Pro Val Asn Leu Lys
        16530                 16535                 16540           1
Val Thr Glu Ile Thr Lys Asp Ser Val Ser Ile Thr Trp Glu Pro Pro
6545               16550                 16555                 16560
Leu Leu Asp Gly Gly Ser Lys Ile Lys Asn Tyr Ile Val Glu Lys Arg
          16565                 16570                 16575
Glu Ala Thr Arg Lys Ser Tyr Ala Ala Val Val Thr Asn Cys His Lys
          16580                 16585                 16590
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Asn Ser Trp Lys Ile Asp Gln Leu Gln Glu Gly Cys Ser Tyr Tyr Phe
    16595            16600            16605
Arg Val Thr Ala Glu Asn Glu Tyr Gly Ile Gly Leu Pro Ala Gln Thr
    16610            16615            16620             1
Ala Asp Pro Ile Lys Val Ala Glu Val Pro Gln Pro Pro Gly Lys Ile
6625             16630            16635            16640
Thr Val Asp Asp Val Thr Arg Asn Ser Val Ser Leu Ser Trp Thr Lys
        16645            16650            16655
Pro Glu His Asp Gly Gly Ser Lys Ile Ile Gln Tyr Ile Val Glu Met
    16660            16665            16670
Gln Ala Lys His Ser Glu Lys Trp Ser Glu Cys Ala Arg Val Lys Ser
    16675            16680            16685
Leu Gln Ala Val Ile Thr Asn Leu Thr Gln Gly Glu Glu Tyr Leu Phe
    16690            16695            16700             1
Arg Val Val Ala Val Asn Glu Lys Gly Arg Ser Asp Pro Arg Ser Leu
6705             16710            16715            16720
Ala Val Pro Ile Val Ala Lys Asp Leu Val Ile Glu Pro Asp Val Lys
        16725            16730            16735
Pro Ala Phe Ser Ser Tyr Ser Val Gln Val Gly Gln Asp Leu Lys Ile
        16740            16745            16750
Glu Val Pro Ile Ser Gly Arg Pro Lys Pro Thr Ile Thr Trp Thr Lys
    16755            16760            16765
Asp Gly Leu Pro Leu Lys Gln Thr Thr Arg Ile Asn Val Thr Asp Ser
    16770            16775            16780             1
Leu Asp Leu Thr Thr Leu Ser Ile Lys Glu Thr His Lys Asp Asp Gly
6785             16790            16795            16800
Gly Gln Tyr Gly Ile Thr Val Ala Asn Val Val Gly Gln Lys Thr Ala
        16805            16810            16815
Ser Ile Glu Ile Val Thr Leu Asp Lys Pro Asp Pro Pro Lys Gly Pro
        16820            16825            16830
Val Lys Phe Asp Asp Val Ser Ala Glu Ser Ile Thr Leu Ser Trp Asn
    16835            16840            16845
Pro Pro Leu Tyr Thr Gly Gly Cys Gln Ile Thr Asn Tyr Ile Val Gln
    16850            16855            16860             1
Lys Arg Asp Thr Thr Thr Thr Val Trp Asp Val Val Ser Ala Thr Val
6865             16870            16875            16880
Ala Arg Thr Thr Leu Lys Val Thr Lys Leu Lys Thr Gly Thr Glu Tyr
        16885            16890            16895
Gln Phe Arg Ile Phe Ala Glu Asn Arg Tyr Gly Gln Ser Phe Ala Leu
    16900            16905            16910
Glu Ser Asp Pro Ile Val Ala Gln Tyr Pro Tyr Lys Glu Pro Gly Pro
    16915            16920            16925
Pro Gly Thr Pro Phe Ala Thr Ala Ile Ser Lys Asp Ser Met Val Ile
    16930            16935            16940             1
Gln Trp His Glu Pro Val Asn Asn Gly Gly Ser Pro Val Ile Gly Tyr
6945             16950            16955            16960
His Leu Glu Arg Lys Glu Arg Asn Ser Ile Leu Trp Thr Lys Val Asn
        16965            16970            16975
Lys Thr Ile Ile His Asp Thr Gln Phe Lys Ala Gln Asn Leu Glu Glu
        16980            16985            16990
Gly Ile Glu Tyr Glu Phe Arg Val Tyr Ala Glu Asn Ile Val Gly Val
    16995            17000            17005
Gly Lys Ala Ser Lys Asn Ser Glu Cys Tyr Val Ala Arg Asp Pro Cys
    17010            17015            17020             1
Asp Pro Pro Gly Thr Pro Glu Pro Ile Met Val Lys Arg Asn Glu Ile
7025             17030            17035            17040
Thr Leu Gln Trp Thr Lys Pro Val Tyr Asp Gly Gly Ser Met Ile Thr
        17045            17050            17055
Gly Tyr Ile Val Glu Lys Arg Asp Leu Pro Asp Gly Arg Trp Met Lys
    17060            17065            17070
Ala Ser Phe Thr Asn Val Ile Glu Thr Gln Phe Thr Val Ser Gly Leu
    17075            17080            17085
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Thr Glu Asp Gln Arg Tyr Glu Phe Arg Val Ile Ala Lys Asn Ala Ala
    17090               17095               17100               1
Gly Ala Ile Ser Lys Pro Ser Asp Ser Thr Gly Pro Ile Thr Ala Lys
7105            17110               17115               17120
Asp Glu Val Glu Leu Pro Arg Ile Ser Met Asp Pro Lys Phe Arg Asp
                17125               17130               17135
Thr Ile Val Val Asn Ala Gly Glu Thr Phe Arg Leu Glu Ala Asp Val
        17140               17145               17150
His Gly Lys Pro Leu Pro Thr Ile Glu Trp Leu Arg Gly Asp Lys Glu
        17155               17160               17165
Ile Glu Glu Ser Ala Arg Cys Glu Ile Lys Asn Thr Asp Phe Lys Ala
    17170               17175               17180               1
Leu Leu Ile Val Lys Asp Ala Ile Arg Ile Asp Gly Gly Gln Tyr Ile
7185            17190               17195               17200
Leu Arg Ala Ser Asn Val Ala Gly Ser Lys Ser Phe Pro Val Asn Val
                17205               17210               17215
Lys Val Leu Asp Arg Pro Gly Pro Glu Gly Pro Val Gln Val Thr
    17220               17225               17230
Gly Val Thr Ser Glu Lys Cys Ser Leu Thr Trp Ser Pro Pro Leu Gln
    17235               17240               17245
Asp Gly Gly Ser Asp Ile Ser His Tyr Val Val Glu Lys Arg Glu Thr
    17250               17255               17260               1
Ser Arg Leu Ala Trp Thr Val Val Ala Ser Glu Val Val Thr Asn Ser
7265            17270               17275               17280
Leu Lys Val Thr Lys Leu Leu Glu Gly Asn Glu Tyr Val Phe Arg Ile
        17285               17290               17295
Met Ala Val Asn Lys Tyr Gly Val Gly Glu Pro Leu Glu Ser Ala Pro
        17300               17305               17310
Val Leu Met Lys Asn Pro Phe Val Leu Pro Gly Pro Pro Lys Ser Leu
        17315               17320               17325
Glu Val Thr Asn Ile Ala Lys Asp Ser Met Thr Val Cys Trp Asn Arg
    17330               17335               17340               1
Pro Asp Ser Asp Gly Gly Ser Glu Ile Ile Gly Tyr Ile Val Glu Lys
7345            17350               17355               17360
Arg Asp Arg Ser Gly Ile Arg Trp Ile Lys Cys Asn Lys Arg Arg Ile
        17365               17370               17375
Thr Asp Leu Arg Leu Arg Val Thr Gly Leu Thr Glu Asp His Glu Tyr
        17380               17385               17390
Glu Phe Arg Val Ser Ala Glu Asn Ala Ala Gly Val Gly Glu Pro Ser
    17395               17400               17405
Pro Ala Thr Val Tyr Tyr Lys Ala Cys Asp Pro Val Phe Lys Pro Gly
    17410               17415               17420               1
Pro Pro Thr Asn Ala His Ile Val Asp Thr Thr Lys Asn Ser Ile Thr
7425            17430               17435               17440
Leu Ala Trp Gly Lys Pro Ile Tyr Asp Gly Gly Ser Glu Ile Leu Gly
        17445               17450               17455
Tyr Val Val Glu Ile Cys Lys Ala Asp Glu Glu Glu Trp Gln Ile Val
        17460               17465               17470
Thr Pro Gln Thr Gly Leu Arg Val Thr Arg Phe Glu Ile Ser Lys Leu
    17475               17480               17485
Thr Glu His Gln Glu Tyr Lys Ile Arg Val Cys Ala Leu Asn Lys Val
    17490               17495               17500               1
Gly Leu Gly Glu Ala Thr Ser Val Pro Gly Thr Val Lys Pro Glu Asp
7505            17510               17515               17520
Lys Leu Glu Ala Pro Glu Leu Asp Leu Asp Ser Glu Leu Arg Lys Gly
        17525               17530               17535
Ile Val Val Arg Ala Gly Gly Ser Ala Arg Ile His Ile Pro Phe Lys
        17540               17545               17550
Gly Arg Pro Met Pro Glu Ile Thr Trp Ser Arg Glu Glu Gly Glu Phe
        17555               17560               17565
Thr Asp Lys Val Gln Ile Glu Lys Gly Val Asn Tyr Thr Gln Leu Ser
    17570               17575               17580               1
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Ile Asp Asn Cys Asp Arg Asn Asp Ala Gly Lys Tyr Ile Leu Lys Leu
7585              17590              17595                   17600
Glu Asn Ser Ser Gly Ser Lys Ser Ala Phe Val Thr Val Lys Val Leu
            17605              17610              17615
Asp Thr Pro Gly Pro Pro Gln Asn Leu Ala Val Lys Glu Val Arg Lys
       17620              17625              17630
Asp Ser Ala Phe Leu Val Trp Glu Pro Pro Ile Ile Asp Gly Gly Ala
       17635              17640              17645
Lys Val Lys Asn Tyr Val Ile Asp Lys Arg Glu Ser Thr Arg Lys Ala
   17650              17655              17660                   1
Tyr Ala Asn Val Ser Ser Lys Cys Ser Lys Thr Ser Phe Lys Val Glu
7665              17670              17675                   17680
Asn Leu Thr Glu Gly Ala Ile Tyr Tyr Phe Arg Val Met Ala Glu Asn
            17685              17690              17695
Glu Phe Gly Val Gly Val Pro Val Glu Thr Val Asp Ala Val Lys Ala
        17700              17705              17710
Ala Glu Pro Pro Ser Pro Pro Gly Lys Val Thr Leu Thr Asp Val Ser
       17715              17720              17725
Gln Thr Ser Ala Ser Leu Met Trp Glu Lys Pro Glu His Asp Gly Gly
   17730              17735              17740                   1
Ser Arg Val Leu Gly Tyr Val Val Glu Met Gln Pro Lys Gly Thr Glu
7745              17750              17755                   17760
Lys Trp Ser Ile Val Ala Glu Ser Lys Val Cys Asn Ala Val Val Thr
            17765              17770              17775
Gly Leu Ser Ser Gly Gln Glu Tyr Gln Phe Arg Val Lys Ala Tyr Asn
        17780              17785              17790
Glu Lys Gly Lys Ser Asp Pro Arg Val Leu Gly Val Pro Val Ile Ala
   17795              17800              17805
Lys Asp Leu Thr Ile Gln Pro Ser Leu Lys Leu Pro Phe Asn Thr Tyr
   17810              17815              17820                   1
Ser Ile Gln Ala Gly Glu Asp Leu Lys Ile Glu Ile Pro Val Ile Gly
7825              17830              17835                   17840
Arg Pro Arg Pro Asn Ile Ser Trp Val Lys Asp Gly Glu Pro Leu Lys
            17845              17850              17855
Gln Thr Thr Arg Val Asn Val Glu Glu Thr Ala Thr Ser Thr Val Leu
        17860              17865              17870
His Ile Lys Glu Gly Asn Lys Asp Asp Phe Gly Lys Tyr Thr Val Thr
   17875              17880              17885
Ala Thr Asn Ser Ala Gly Thr Ala Thr Glu Asn Leu Ser Val Ile Val
   17890              17895              17900                   1
Leu Glu Lys Pro Gly Pro Pro Val Gly Pro Val Arg Phe Asp Glu Val
7905              17910              17915                   17920
Ser Ala Asp Phe Val Val Ile Ser Trp Glu Pro Pro Ala Tyr Thr Gly
        17925              17930              17935
Gly Cys Gln Ile Ser Asn Tyr Ile Val Glu Lys Arg Asp Thr Thr Thr
        17940              17945              17950
Thr Thr Trp His Met Val Ser Ala Thr Val Ala Arg Thr Thr Ile Lys
   17955              17960              17965
Ile Thr Lys Leu Lys Thr Gly Thr Glu Tyr Gln Phe Arg Ile Phe Ala
   17970              17975              17980                   1
Glu Asn Arg Tyr Gly Lys Ser Ala Pro Leu Asp Ser Lys Ala Val Ile
7985              17990              17995                   18000
Val Gln Tyr Pro Phe Lys Glu Pro Gly Pro Pro Gly Thr Pro Phe Val
            18005              18010              18015
Thr Ser Ile Ser Lys Asp Gln Met Leu Val Gln Trp His Glu Pro Val
        18020              18025              18030
Asn Asp Gly Gly Thr Lys Ile Ile Gly Tyr His Leu Glu Gln Lys Glu
        18035              18040              18045
Lys Asn Ser Ile Leu Trp Val Lys Leu Asn Lys Thr Pro Ile Gln Asp
   18050              18055              18060                   1
Thr Lys Phe Lys Thr Thr Gly Leu Asp Glu Gly Leu Glu Tyr Glu Phe
8065              18070              18075              18080
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Lys Val Ser Ala Glu Asn Ile Val Gly Ile Gly Lys Pro Ser Lys Val
        18085                 18090                 18095
Ser Glu Cys Phe Val Ala Arg Asp Pro Cys Asp Pro Pro Gly Arg Pro
        18100                 18105                 18110
Glu Ala Ile Val Ile Thr Arg Asn Asn Val Thr Leu Lys Trp Lys Lys
        18115        .        18120                 18125
Pro Ala Tyr Asp Gly Gly Ser Lys Ile Thr Gly Tyr Ile Val Glu Lys
    18130                 18135                 18140                 1
Lys Asp Leu Pro Asp Gly Arg Trp Met Lys Ala Ser Phe Thr Asn Val
8145                 18150                 18155        .        18160
Leu Glu Thr Glu Phe Thr Val Ser Gly Leu Val Glu Asp Gln Arg Tyr
        18165                 18170                 18175
Glu Phe Arg Val Ile Ala Arg Asn Ala Ala Gly Asn Phe Ser Glu Pro
        18180                 18185                 18190
Ser Asp Ser Ser Gly Ala Ile Thr Ala Arg Asp Glu Ile Asp Ala Pro
        18195                 18200                 18205
Asn Ala Ser Leu Asp Pro Lys Tyr Lys Asp Val Ile Val Val His Ala
        18210                 18215                 18220                 1
Gly Glu Thr Phe Val Leu Glu Ala Asp Ile Arg Gly Lys Pro Ile Pro
8225                 18230                 18235                 18240
Asp Val Val Trp Ser Lys Asp Gly Lys Glu Leu Glu Glu Thr Ala Ala
    .18245                 18250                 18255
Arg Met Glu Ile Lys Ser Thr Ile Gln Lys Thr Thr Leu Val Val Lys
        18260                 18265        .        18270
Asp Cys Ile Arg Thr Asp Gly Gly Gln Tyr Ile Leu Lys Leu Ser Asn
        18275        .        18280                 18285
Val Gly Gly Thr Lys Ser Ile Pro Ile Thr Val Lys Val Leu Asp Arg
        18290                 18295                 18300                 1
Pro Gly Ser Pro Glu Gly Pro Leu Lys Val Thr Gly Val Thr Ala Glu
8305                 18310                 18315                 18320
Lys Cys Tyr Leu Ala Trp Asn Pro Pro Leu Gln Asp Gly Gly Ala Asn
        .18325                 18330                 18335
Ile Ser His Tyr Ile Ile Glu Lys Arg Glu Thr Ser Arg Leu Ser Trp
        18340                 18345                 18350
Thr Gln Val Ser Thr Glu Val Gln Ala Leu Asn Tyr Lys Val Thr Lys
        18355                 18360                 18365       ·
Leu Leu Pro Gly Asn Glu Tyr Ile Phe Arg Val Met Ala Val Asn Lys
        18370                 18375                 18380                 1
Tyr Gly Ile Gly Glu Pro Leu Glu Ser Gly Pro Val Thr·Ala Cys Asn
8385                 18390                 18395                 18400
Pro Tyr Lys Pro Pro Gly Pro Pro Ser Thr Pro Glu Val Ser Ala Ile
        18405                 18410                 18415
Thr Lys Asp Ser Met Val Val Thr Trp Ala Arg Pro Val Asp Asp Gly
        18420                 18425                 18430
Gly Thr Glu Ile Glu Gly Tyr Ile Leu Glu Lys Arg Asp Lys Glu Gly
        18435                 18440                 18445
Val Arg Trp Thr Lys Cys Asn Lys Lys Thr Leu Thr Asp Leu Arg Leu
        18450                 18455                 18460                 1
Arg Val Thr Gly Leu Thr Glu Gly His Ser Tyr Glu Phe Arg Val Ala
8465                 18470                 18475                 18480
Ala Glu Asn Ala Ala Gly Val Gly Glu Pro Ser Glu Pro Ser Val Phe
        18485                 18490                 18495
Tyr Arg Ala Cys Asp Ala Leu Tyr Pro Pro Gly Pro Pro Ser Asn Pro
        18500                 18505                 18510
Lys Val Thr Asp Thr Ser Arg Ser Ser Val Ser Leu Ala Trp Ser Lys
        18515                 18520                 18525
Pro Ile Tyr Asp Gly Gly Ala Pro Val Lys Gly Tyr Val Val Glu Val
        18530                 18535                 18540                 1
Lys Glu Ala Ala Ala Asp Glu Trp Thr Thr Cys Thr Pro Pro Thr Gly
8545                 18550                 18555                 18560
Leu Gln Gly Lys Gln Phe Thr Val Thr Lys Leu Lys Glu Asn Thr Glu
            18565                 18570                 18575
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Tyr Asn Phe Arg Ile Cys Ala Ile Asn Ser Glu Gly Val Gly Glu Pro
        18580   18585   18590
Ala Thr Leu Pro Gly Ser Val Val Ala Gln Glu Arg Ile Glu Pro Pro
        18595   18600   18605
Glu Ile Glu Leu Asp Ala Asp Leu Arg Lys Val Val Val Leu Arg Ala
    18610   18615   18620   1
Ser Ala Thr Leu Arg Leu Phe Val Thr Ile Lys Gly Arg Pro Glu Pro
8625   18630   18635   18640
Glu Val Lys Trp Glu Lys Ala Glu Gly Ile Leu Thr Asp Arg Ala Gln
        18645   18650   18655
Ile Glu Val Thr Ser Ser Phe Thr Met Leu Val Ile Asp Asn Val Thr
        18660   18665   18670
Arg Phe Asp Ser Gly Arg Tyr Asn Leu Thr Leu Glu Asn Asn Ser Gly
        18675   18680   18685
Ser Lys Thr Ala Phe Val Asn Val Arg Val Leu Asp Ser Pro Ser Ala
    18690   18695   18700   1
Pro Val Asn Leu Thr Ile Arg Glu Val Lys Lys Asp Ser Val Thr Leu
8705   18710   18715   18720
Ser Trp Glu Pro Pro Leu Ile Asp Gly Gly Ala Lys Ile Thr Asn Tyr
        18725   18730   18735
Ile Val Glu Lys Arg Glu Thr Thr Arg Lys Ala Tyr Ala Thr Ile Thr
        18740   18745   18750
Asn Asn Cys Thr Lys Thr Thr Phe Arg Ile Glu Asn Leu Gln Glu Gly
        18755   18760   18765
Cys Ser Tyr Tyr Phe Arg Val Leu Ala Ser Asn Glu Tyr Gly Ile Gly
    18770   18775   18780   1
Leu Pro Ala Glu Thr Thr Glu Pro Val Lys Val Ser Glu Pro Pro Leu
8785   18790   18795   18800
Pro Pro Gly Arg Val Thr Leu Val Asp Val Thr Arg Asn Thr Ala Thr
        18805   18810   18815
Ile Lys Trp Glu Lys Pro Glu Ser Asp Gly Gly Ser Lys Ile Thr Gly
        18820   18825   18830
Tyr Val Val Glu Met Gln Thr Lys Gly Ser Glu Lys Trp Ser Thr Cys
        18835   18840   18845
Thr Gln Val Lys Thr Leu Glu Ala Thr Ile Ser Gly Leu Thr Ala Gly
    18850   18855   18860   1
Glu Glu Tyr Val Phe Arg Val Ala Ala Val Asn Glu Lys Gly Arg Ser
8865   18870   18875   18880
Asp Pro Arg Gln Leu Gly Val Pro Val Ile Ala Arg Asp Ile Glu Ile
        18885   18890   18895
Lys Pro Ser Val Glu Leu Pro Phe His Thr Phe Asn Val Lys Ala Arg
        18900   18905   18910
Glu Gln Leu Lys Ile Asp Val Pro Phe Lys Gly Arg Pro Gln Ala Thr
        18915   18920   18925
Val Asn Trp Arg Lys Asp Gly Gln Thr Leu Lys Glu Thr Thr Arg Val
    18930   18935   18940   1
Asn Val Ser Ser Ser Lys Thr Val Thr Ser Leu Ser Ile Lys Glu Ala
8945   18950   18955   18960
Ser Lys Glu Asp Val Gly Thr Tyr Glu Leu Cys Val Ser Asn Ser Ala
        18965   18970   18975
Gly Ser Ile Thr Val Pro Ile Thr Ile Ile Val Leu Asp Arg Pro Gly
        18980   18985   18990
Pro Pro Gly Pro Ile Arg Ile Asp Glu Val Ser Cys Asp Ser Ile Thr
        18995   19000   19005
Ile Ser Trp Asn Pro Pro Glu Tyr Asp Gly Gly Cys Gln Ile Ser Asn
    19010   19015   19020   1
Tyr Ile Val Glu Lys Lys Glu Thr Thr Ser Thr Thr Trp His Ile Val
9025   19030   19035   19040
Ser Gln Ala Val Ala Arg Thr Ser Ile Lys Ile Val Arg Leu Thr Thr
        19045   19050   19055
Gly Ser Glu Tyr Gln Phe Arg Val Cys Ala Glu Asn Arg Tyr Gly Lys
        19060   19065   19070

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Ser Ser Tyr Ser Glu Ser Ser Ala Val Val Ala Glu Tyr Pro Phe Ser
    19075                 19080                 19085
Pro Pro Gly Pro Pro Gly Thr Pro Lys Val Val His Ala Thr Lys Ser
    19090                 19095                 19100             1
Thr Met Leu Val Thr Trp Gln Val Pro Val Asn Asp Gly Gly Ser Arg
9105                  19110                 19115             19120
Val Ile Gly Tyr His Leu Glu Tyr Lys Glu Arg Ser Ser Ile Leu Trp
    19125                 19130                 19135
Ser Lys Ala Asn Lys Ile Leu Ile Ala Asp Thr Gln Val Lys Val Ser
    19140                 19145                 19150
Gly Leu Asp Glu Gly Leu Met Tyr Glu Tyr Arg Val Tyr Ala Glu Asn
    19155                 19160                 19165
Ile Ala Gly Ile Gly Lys Cys Ser Lys Ser Cys Glu Pro Val Pro Ala
    19170                 19175                 19180             1
Arg Asp Pro Cys Asp Pro Pro Gly Gln Pro Glu Val Thr Asn Ile Thr
9185                  19190                 19195             19200
Arg Lys Ser Val Ser Leu Lys Trp Ser Lys Pro His Tyr Asp Gly Gly
    19205                 19210                 19215
Ala Lys Ile Thr Gly Tyr Ile Val Glu Arg Arg Glu Leu Pro Asp Gly
    19220                 19225                 19230
Arg Trp Leu Lys Cys Asn Tyr Thr Asn Ile Gln Glu Thr Tyr Phe Glu
    19235                 19240                 19245
Val Thr Glu Leu Thr Glu Asp Gln Arg Tyr Glu Phe Arg Val Phe Ala
    19250                 19255                 19260             1
Arg Asn Ala Ala Asp Ser Val Ser Glu Pro Ser Glu Ser Thr Gly Pro
9265                  19270                 19275             19280
Ile Ile Val Lys Asp Asp Val Glu Pro Pro Arg Val Met Met Asp Val
    19285                 19290                 19295
Lys Phe Arg Asp Val Ile Val Val Lys Ala Gly Glu Val Leu Lys Ile
    19300                 19305                 19310
Asn Ala Asp Ile Ala Gly Arg Pro Leu Pro Val Ile Ser Trp Ala Lys
    19315                 19320                 19325
Asp Gly Ile Glu Ile Glu Glu Arg Ala Arg Thr Glu Ile Ile Ser Thr
    19330                 19335                 19340             1
Asp Asn His Thr Leu Leu Thr Val Lys Asp Cys Ile Arg Arg Asp Thr
9345                  19350                 19355             19360
Gly Gln Tyr Val Leu Thr Leu Lys Asn Val Ala Gly Thr Arg Ser Val
    19365                 19370                 19375
Ala Val Asn Cys Lys Val Leu Asp Lys Pro Gly Pro Pro Ala Gly Pro
    19380                 19385                 19390
Leu Glu Ile Asn Gly Leu Thr Ala Glu Lys Cys Ser Leu Ser Trp Gly
    19395                 19400                 19405
Arg Pro Gln Glu Asp Gly Gly Ala Asp Ile Asp Tyr Tyr His Arg Lys
    19410                 19415                 19420             1
Lys Arg Glu Thr Ser His Leu Ala Trp Thr Ile Cys Glu Gly Glu Leu
9425                  19430                 19435             19440
Gln Met Thr Ser Cys Lys Val Thr Lys Leu Leu Lys Gly Asn Glu Tyr
    19445                 19450                 19455
Ile Phe Arg Val Thr Gly Val Asn Lys Tyr Gly Val Gly Glu Pro Leu
    19460                 19465                 19470
Glu Ser Val Ala Ile Lys Ala Leu Asp Pro Phe Thr Val Pro Ser Pro
    19475                 19480                 19485
Pro Thr Ser Leu Glu Ile Thr Ser Val Thr Lys Glu Ser Met Thr Leu
    19490                 19495                 19500             1
Cys Trp Ser Arg Pro Glu Ser Asp Gly Gly Ser Glu Ile Ser Gly Tyr
9505                  19510                 19515             19520
Ile Ile Glu Arg Arg Glu Lys Asn Ser Leu Arg Trp Val Arg Val Asn
    19525                 19530                 19535
Lys Lys Pro Val Tyr Asp Leu Arg Val Lys Ser Thr Gly Leu Arg Glu
    19540                 19545                 19550
Gly Cys Glu Tyr Glu Tyr Arg Val Tyr Ala Glu Asn Ala Ala Gly Leu
    19555                 19560                 19565
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Ser Leu Pro Ser Glu Thr Ser Pro Leu Ile Arg Ala Glu Asp Pro Val
   19570              19575              19580              1
Phe Leu Pro Ser Pro Pro Ser Lys Pro Lys Ile Val Asp Ser Gly Lys
9585              19590              19595              19600
Thr Thr Ile Thr Ile Ala Trp Val Lys Pro Leu Phe Asp Gly Gly Ala
            19605              19610        .      19615
Pro Ile Thr Gly Tyr Thr Val Glu Tyr Lys Lys Ser Asp Asp Thr Asp
            19620              19625              19630
Trp Lys Thr Ser Ile Gln Ser Leu Arg Gly Thr Glu Tyr Thr Ile Ser
            19635              19640              19645
Gly Leu Thr Thr Gly Ala Glu Tyr Val Phe Arg Val Lys Ser Val Asn
   19650              19655              19660              1
Lys Val Gly Ala Ser Asp Pro Ser Asp Ser Ser Asp Pro Gln Ile Ala
9665              19670              19675              19680
Lys Glu Arg Glu Glu Glu Pro Leu Phe Asp Ile Asp Ser Glu Met Arg
            19685              19690              19695
Lys Thr Leu Ile Val Lys Ala Gly Ala Ser Phe Thr Met Thr Val Pro
            19700              19705              19710
Phe Arg Gly Arg Pro Val Pro Asn Val Leu Trp Ser Lys Pro Asp Thr
            19715              19720              19725
Asp Leu Arg Thr Arg Ala Tyr Val Asp Thr Thr Asp Ser Arg Thr Ser
   19730              19735              19740              1
Leu Thr Ile Glu Asn Ala Asn Arg Asn Asp Ser Gly Lys Tyr Thr Leu
9745              19750              19755              19760
Thr Ile Gln Asn Val Leu Ser.Ala Ala Ser Leu Thr Leu Val Val Lys
            19765              19770              19775
Val Leu Asp Thr Pro Gly Pro.Pro Thr Asn Ile Thr Val Gln Asp Val
            19780              19785              19790
Thr Lys Glu Ser Ala Val Leu Ser Trp Asp Val Pro Glu Asn Asp Gly
   19795              19800        .      19805
Gly Ala Pro Val Lys Asn Tyr His Ile Glu Lys Arg Glu Ala Ser Lys
   19810              19815              19820              1
Lys Ala Trp Val Ser Val Thr Asn Asn Cys Asn Arg Leu Ser Tyr Lys
9825              19830              19835              19840
Val Thr Asn Leu Gln Glu Gly Ala Ile Tyr Tyr Phe Arg Val Ser Gly
            19845              19850              19855
Glu Asn Glu Phe Gly Val Gly Ile Pro Ala Glu Thr Lys Glu Gly Val
            19860              19865              19870
Lys Ile Thr Glu Lys Pro Ser Pro Pro Glu Lys Leu Gly Val Thr Ser
   19875              19880              19885
Ile Ser Lys Asp Ser Val Ser Leu Thr Trp Leu Lys Pro Glu His Asp
   19890              19895              19900              1
Gly Gly Ser Arg Ile Val His Tyr Val Val Glu Ala Leu Glu Lys Gly .
9905              19910              19915              19920
Gln Lys Asn Trp Val Lys Cys Ala Val Ala Lys Ser Thr His His Val
            19925              19930              19935
Val Ser Gly Leu Arg Glu Asn Ser Glu Tyr Phe Phe Arg Val Phe Ala
            19940              19945              19950
Glu Asn Gln Ala Gly Leu Ser Asp Pro Arg Glu Leu Leu Leu Pro Val
   19955              19960              19965
Leu Ile Lys Glu Gln Leu Glu Pro Pro Glu Ile Asp Met Lys Asn Phe
   19970              19975              19980              1
Pro Ser His Thr Val Tyr Val Arg Ala Gly Ser Asn Leu Lys Val Asp
9985              19990              19995              20000
Ile Pro Ile Ser Gly Lys Pro Leu Pro Lys Val Thr Leu Ser Arg Asp
            20005              20010              20015
Gly Val Pro Leu Lys Ala Thr Met Arg Phe Asn Thr Glu Ile Thr Ala
            20020              20025              20030
Glu Asn Leu Thr Ile Asn Leu Lys Glu Ser Val Thr Ala Asp Ala Gly
   20035              20040              20045
Arg Tyr Glu Ile Thr Ala Ala Asn Ser Ser Gly Thr Thr Lys Ala Phe
   20050              20055              20060              2
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Ile Asn Ile Val Val Leu Asp Arg Pro Gly Pro Pro Thr Gly Pro Val
0065             20070               20075               20080
Val Ile Ser Asp Ile Thr Glu Glu Ser Val Thr Leu Lys Trp Glu Pro
            20085               20090               20095
Pro Lys Tyr Asp Gly Gly Ser Gln Val Thr Asn Tyr Ile Leu Leu Lys
            20100               20105               20110
Arg Glu Thr Ser Thr Ala Val Trp Thr Glu Val Ser Ala Thr Val Ala
            20115               20120               20125
Arg Thr Met Met Lys Val Met Lys Leu Thr Thr Gly Glu Glu Tyr Gln
            20130               20135               20140             2
Phe Arg Ile Lys Ala Glu Asn Arg Phe Gly Ile Ser Asp His Ile Asp
0145             20150               20155               20160
Ser Ala Cys Val Thr Val Lys Leu Pro Tyr Thr Thr Pro Gly Pro Pro
            20165               20170               20175
Ser Thr Pro Trp Val Thr Asn Val Thr Arg Glu Ser Ile Thr Val Gly
            20180               20185               20190
Trp His Glu Pro Val Ser Asn Gly Gly Ser Ala Val Val Gly Tyr His
            20195               20200               20205
Leu Glu Met Lys Asp Arg Asn Ser Ile Leu Trp Gln Lys Ala Asn Lys
            20210               20215               20220             2
Leu Val Ile Arg Thr Thr His Phe Lys Val Thr Thr Ile Ser Ala Gly
0225             20230               20235               20240
Leu Ile Tyr Glu Phe Arg Val Tyr Ala Glu Asn Ala Ala Gly Val Gly
            20245               20250               20255
Lys Pro Ser His Pro Ser Glu Pro Val Leu Ala Ile Asp Ala Cys Glu
            20260               20265               20270
Pro Pro Arg Asn Val Arg Ile Thr Asp Ile Ser Lys Asn Ser Val Ser
            20275               20280               20285
Leu Ser Trp Gln Gln Pro Ala Phe Asp Gly Gly Ser Lys Ile Thr Gly
            20290               20295               20300             2
Tyr Ile Val Glu Arg Arg Asp Leu Pro Asp Gly Arg Trp Thr Lys Ala
0305             20310               20315               20320
Ser Phe Thr Asn Val Thr Glu Thr Gln Phe Thr Ile Ser Gly Leu Thr
            20325               20330               20335
Gln Asn Ser Gln Tyr Glu Phe Arg Val Phe Ala Arg Asn Ala Val Gly
            20340               20345               20350
Ser Ile Ser Asn Pro Ser Glu Val Val Gly Pro Ile Thr Cys Ile Asp
            20355               20360               20365
Ser Tyr Gly Gly Pro Val Ile Asp Leu Pro Leu Glu Tyr Thr Glu Val
            20370               20375               20380             2
Val Lys Tyr Arg Ala Gly Thr Ser Val Lys Leu Arg Ala Gly Ile Ser
0385             20390               20395               20400
Gly Lys Pro Ala Pro Thr Ile Glu Trp Tyr Lys Asp Asp Lys Glu Leu
            20405               20410               20415
Gln Thr Asn Ala Leu Val Cys Val Glu Asn Thr Thr Asp Leu Ala Ser
            20420               20425               20430
Ile Leu Ile Lys Asp Ala Asp Arg Leu Asn Ser Gly Cys Tyr Glu Leu
            20435       .       20440               20445
Lys Leu Arg Asn Ala Met Ala Ser Ala Ser Ala Thr Ile Arg Val Gln
            20450               20455               20460             2
Ile Leu Asp Lys Pro Gly Pro Pro Gly Gly Pro Ile Glu Phe Lys Thr
0465             20470               20475               20480
Val Thr Ala Glu Lys Ile Thr Leu Leu Trp Arg Pro Pro Ala Asp Asp
            20485               20490               20495
Gly Gly Ala Lys Ile Thr His Tyr Ile Val Glu Lys Arg Glu Thr Ser
            20500               20505               20510
Arg Val Val Trp Ser Met Val Ser Glu His Leu Glu Glu Cys Ile Ile
            20515               20520               20525
Thr Thr Thr Lys Ile Ile Lys Gly Asn Glu Tyr Ile Phe Arg Val Arg
            20530               20535               20540             2
Ala Val Asn Lys Tyr Gly Ile Gly Glu Pro Leu Glu Ser Asp Ser Val
0545             20550               20555               20560
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Val Ala Lys Asn Ala Phe Val Thr Pro Gly Pro Pro Gly Ile Pro Glu
            20565               20570               20575
Val Thr Lys Ile Thr Lys Asn Ser Met Thr Val Val Trp Ser Arg Pro
        20580               20585               20590
Ile Ala Asp Gly Gly Ser Asp Ile Ser Gly Tyr Phe Leu Glu Lys Arg
            20595               20600               20605
Asp Lys Lys Ser Leu Gly Trp Phe Lys Val Leu Lys Glu Thr Ile Arg
    20610               20615               20620               2
Asp Thr Arg Gln Lys Val Thr Gly Leu Thr Glu Asn Ser Asp Tyr Gln
0625               20630               20635               20640
Tyr Arg Val Cys Ala Val Asn Ala Ala Gly Gln Gly Pro Phe Ser Glu
            20645               20650               20655
Pro Ser Glu Phe Tyr Lys Ala Ala Asp Pro Ile Asp Pro Pro Gly Pro
            20660               20665               20670
Pro Ala Lys Ile Arg Ile Ala Asp Ser Thr Lys Ser Ser Ile Thr Leu
        20675               20680               20685
Gly Trp Ser Lys Pro Val Tyr Asp Gly Gly Ser Ala Val Thr Gly Tyr
    20690               20695               20700               2
Val Val Glu Ile Arg Gln Gly Glu Glu Glu Glu Trp Thr Thr Val Ser
0705               20710               20715               20720
Thr Lys Gly Glu Val Arg Thr Thr Glu Tyr Val Val Ser Asn Leu Lys
            20725               20730               20735
Pro Gly Val Asn Tyr Tyr Phe Arg Val Ser Ala Val Asn Cys Ala Gly
        20740               20745               20750
Gln Gly Glu Pro Ile Glu Met Asn Glu Pro Val Gln Ala Lys Asp Ile
        20755               20760               20765
Leu Glu Ala Pro Glu Ile Asp Leu Asp Val Ala Leu Arg Thr Ser Val
    20770               20775               20780               2
Ile Ala Lys Ala Gly Glu Asp Val Gln Val Leu Ile Pro Phe Lys Gly
0785               20790               20795               20800
Arg Pro Pro Pro Thr Val Thr Trp Arg Lys Asp Glu Lys Asn Leu Gly
            20805               20810               20815
Ser Asp Ala Arg Tyr Ser Ile Glu Asn Thr Asp Ser Ser Ser Leu Leu
        20820               20825               20830
Thr Ile Pro Gln Val Thr Arg Asn Asp Thr Gly Lys Tyr Ile Leu Thr
    20835               20840               20845
Ile Glu Asn Gly Val Gly Glu Pro Lys Ser Ser Thr Val Ser Val Lys
    20850               20855               20860               2
Val Leu Asp Thr Pro Ala Ala Cys Gln Lys Leu Gln Val Lys His Val
0865               20870               20875               20880
Ser Arg Gly Thr Val Thr Leu Leu Trp Asp Pro Pro Leu Ile Asp Gly
            20885               20890               20895
Gly Ser Pro Ile Ile Asn Tyr Val Ile Glu Lys Arg Asp Ala Thr Lys
    20900               20905               20910
Arg Thr Trp Ser Val Val Ser His Lys Cys Ser Ser Thr Ser Phe Lys
    20915               20920               20925
Leu Ile Asp Leu Ser Glu Lys Thr Pro Phe Phe Phe Arg Val Leu Ala
    20930               20935               20940               2
Glu Asn Glu Ile Gly Ile Gly Glu Pro Cys Glu Thr Thr Glu Pro Val
0945               20950               20955               20960
Lys Ala Ala Glu Val Pro Ala Pro Ile Arg Asp Leu Ser Met Lys Asp
            20965               20970               20975
Ser Thr Lys Thr Ser Val Ile Leu Ser Trp Thr Lys Pro Asp Phe Asp
        20980               20985               20990
Gly Gly Ser Val Ile Thr Glu Tyr Val Val Glu Arg Lys Gly Lys Gly
        20995               21000               21005
Glu Gln Thr Trp Ser His Ala Gly Ile Ser Lys Thr Cys Glu Ile Glu
    21010               21015               21020               2
Val Ser Gln Leu Lys Glu Gln Ser Val Leu Glu Phe Arg Val Phe Ala
1025               21030               21035               21040
Lys Asn Glu Lys Gly Leu Ser Asp Pro Val Thr Ile Gly Pro Ile Thr
            21045               21050               21055
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Val Lys Glu Leu Ile Ile Thr Pro Glu Val Asp Leu Ser Asp Ile Pro
          21060   21065   21070
Gly Ala Gln Val Thr Val Arg Ile Gly His Asn Val His Leu Glu Leu
          21075   21080   21085
Pro Tyr Lys Gly Lys Pro Lys Pro Ser Ile Ser Trp Leu Lys Asp Gly
          21090   21095   21100   2
Leu Pro Leu Lys Glu Ser Glu Phe Val Arg Phe Ser Lys Thr Glu Asn
1105   21110   21115   21120
Lys Ile Thr Leu Ser Ile Lys Asn Ala Lys Lys Glu His Gly Gly Lys
          21125   21130   21135
Tyr Thr Val Ile Leu Asp Asn Ala Val Cys Arg Ile Ala Val Pro Ile
          21140   21145   21150
Thr Val Ile Thr Leu Gly Pro Pro Ser Lys Pro Lys Gly Pro Ile Arg
          21155   21160   21165
Phe Asp Glu Ile Lys Ala Asp Ser Val Ile Leu Ser Trp Asp Val Pro
          21170   21175   21180   2
Glu Asp Asn Gly Gly Gly Glu Ile Thr Cys Tyr Ser Ile Glu Lys Arg
1185   21190   21195   21200
Glu Thr Ser Gln Thr Asn Trp Lys Met Val Cys Ser Ser Val Ala Arg
          21205   21210   21215
Thr Thr Phe Lys Val Pro Asn Leu Val Lys Asp Ala Glu Tyr Gln Phe
          21220   21225   21230
Arg Val Arg Ala Glu Asn Arg Tyr Gly Val Ser Gln Pro Leu Val Ser
          21235   21240   21245
Ser Ile Ile Val Ala Lys His Gln Phe Arg Ile Pro Gly Pro Pro Gly
          21250   21255   21260   2
Lys Pro Val Ile Tyr Asn Val Thr Ser Asp Gly Met Ser Leu Thr Trp
1265   21270   21275   21280
Asp Ala Pro Val Tyr Asp Gly Gly Ser Glu Val Thr Gly Phe His Val
          21285   21290   21295
Glu Lys Lys Glu Arg Asn Ser Ile Leu Trp Gln Lys Val Asn Thr Ser
          21300   21305   21310
Pro Ile Ser Gly Arg Glu Tyr Arg Ala Thr Gly Leu Val Glu Gly Leu
          21315   21320   21325
Asp Tyr Gln Phe Arg Val Tyr Ala Glu Asn Ser Ala Gly Leu Ser Ser
          21330   21335   21340   2
Pro Ser Asp Pro Ser Lys Phe Thr Leu Ala Val Ser Pro Val Asp Pro
1345   21350   21355   21360
Pro Gly Thr Pro Asp Tyr Ile Asp Val Thr Arg Glu Thr Ile Thr Leu
          21365   21370   21375
Lys Trp Asn Pro Pro Leu Arg Asp Gly Gly Ser Lys Ile Val Gly Tyr
          21380   21385   21390
Ser Ile Glu Lys Arg Gln Gly Asn Glu Arg Trp Val Arg Cys Asn Phe
          21395   21400   21405
Thr Asp Val Ser Glu Cys Gln Tyr Thr Val Thr Gly Leu Ser Pro Gly
          21410   21415   21420   2
Asp Arg Tyr Glu Phe Arg Ile Ile Ala Arg Asn Ala Val Gly Thr Ile
1425   21430   21435   21440
Ser Pro Pro Ser Gln Ser Ser Gly Ile Ile Met Thr Arg Asp Glu Asn
          21445   21450   21455
Val Pro Pro Ile Val Glu Phe Gly Pro Glu Tyr Phe Asp Gly Leu Ile
          21460   21465   21470
Ile Lys Ser Gly Glu Ser Leu Arg Ile Lys Ala Leu Val Gln Gly Arg
          21475   21480   21485
Pro Val Pro Arg Val Thr Trp Phe Lys Asp Gly Val Glu Ile Glu Lys
          21490   21495   21500   2
Arg Met Asn Met Glu Ile Thr Asn Val Leu Gly Ser Thr Ser Leu Phe
1505   21510   21515   21520
Val Arg Asp Ala Thr Arg Asp His Arg Gly Val Tyr Thr Val Glu Ala
          21525   21530   21535
Lys Asn Ala Ser Gly Ser Ala Lys Ala Glu Ile Lys Val Lys Val Gln
          21540   21545   21550

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Asp Thr Pro Gly Lys Val Val Gly Pro Ile Arg Phe Thr Asn Ile Thr
        21555              21560              21565
Gly Glu Lys Met Thr Leu Trp Trp Asp Ala Pro Leu Asn Asp Gly Cys
   21570              21575              21580              2
Ala Pro Ile Thr His Tyr Ile Ile Glu Lys Arg Glu Thr Ser Arg Leu
1585              21590              21595              21600
Ala Trp Ala Leu Ile Glu Asp Lys Cys Glu Ala Gln Ser Tyr Thr Ala
        21605              21610              21615
Ile Lys Leu Ile Asn Gly Asn Glu Tyr Gln Phe Arg Val Ser Ala Val
        21620              21625              21630
Asn Lys Phe Gly Val Gly Arg Pro Leu Asp Ser Asp Pro Val Val Ala
   21635              21640              21645
Gln Ile Gln Tyr Thr Val Pro Asp Ala Pro Gly Ile Pro Glu Pro Ser
   21650              21655              21660              2
Asn Ile Thr Gly Asn Ser Ile Thr Leu Thr Trp Ala Arg Pro Glu Ser
1665              21670              21675              21680
Asp Gly Gly Ser Glu Ile Gln Gln Tyr Ile Leu Glu Arg Arg Glu Lys
        21685              21690              21695
Lys Ser Thr Arg Trp Val Lys Val Ile Ser Lys Arg Pro Ile Ser Glu
        21700              21705              21710
Thr Arg Phe Lys Val Thr Gly Leu Thr Glu Gly Asn Glu Tyr Glu Phe
   21715              21720              21725
His Val Met Ala Glu Asn Ala Ala Gly Val Gly Pro Ala Ser Gly Ile
   21730        ·      21735              21740              2
Ser Arg Leu Ile Lys Cys Arg Glu Pro Val Asn Pro Pro Gly Pro Pro
1745              21750              21755              21760
Thr Val Val Lys Val Thr Asp Thr Ser Lys Thr Thr Val Ser Leu Glu
        21765              21770       ·      21775
Trp.Ser Lys Pro Val Phe Asp Gly Gly Met Glu Ile Ile Gly Tyr Ile
        21780              21785              21790
Ile Glu Met Cys Lys Thr Asp Leu Gly Asp Trp His Lys Val Asn Ala
     ·  21795              21800              21805
Glu Ala Cys Val Lys Thr Arg Tyr Thr Val Thr Asp Leu Gln Ala Gly
   21810              21815              21820              2
Glu Glu Tyr Lys Phe Arg Val Ser Ala Ile Asn Gly Ala Gly Lys Gly
1825              21830              21835              21840
Asp Ser Cys Glu Val Thr Gly Thr Ile Lys Ala Val Asp Arg Leu Thr
        21845              21850              21855
Ala Pro Glu Leu Asp Ile Asp Ala Asn Phe Lys Gln Thr.His Val Val
        21860              21865              21870
Arg Ala Gly Ala Ser Ile Arg Leu Phe Ile Ala Tyr Gln Gly Arg Pro
   21875              21880              21885
Thr Pro Thr Ala Val Trp Ser Lys Pro Asp Ser Asn Leu Ser Leu Arg
   21890              21895              21900              2
Ala Asp Ile His Thr Thr Asp Ser Phe Ser Thr Leu Thr Val Glu Asn
1905              21910              21915              21920
Cys Asn Arg Asn Asp Ala Gly Lys Tyr Thr Leu Thr Val Glu Asn Asn
        21925              21930              21935
Ser Gly Ser Lys Ser Ile Thr Phe Thr Val Lys Val Leu Asp Thr Pro
     21940       ·      21945              21950
Gly Pro Pro Gly Pro Ile Thr Phe Lys Asp Val Thr Arg Gly Ser Ala
   21955              21960              21965
Thr Leu Met Trp Asp Ala Pro Leu Leu Asp Gly Gly Ala Arg Ile His
   21970              21975              21980              2
His Tyr Val Val Glu Lys Arg Glu Ala Ser Arg Arg Ser Trp Gln Val
1985              21990              21995              22000
Ile Ser Glu Lys Cys Thr Arg Gln Ile Phe Lys Val Asn Asp Leu Ala
        22005              22010              22015
Glu Gly Val Pro Tyr Tyr Phe Arg Val Ser Ala Val Asn Glu Tyr Gly
     22020              22025              22030
Val Gly Glu Pro Tyr Glu Met Pro Glu Pro Ile Val·Ala Thr Glu Gln
   22035              22040              22045
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Pro Ala Pro Pro Arg Arg Leu Asp Val Val Asp Thr Ser Lys Ser Ser
    22050             22055             22060                 2
Ala Val Leu Ala Trp Leu Lys Pro Asp His Asp Gly Gly Ser Arg Ile
2065          22070         22075             22080
Thr Gly Tyr Leu Leu Glu Met Arg Gln Lys Gly Ser Asp Leu Trp Val
            22085             22090             22095
Glu Ala Gly His Thr Lys Gln Leu Thr Phe Thr Val Glu Arg Leu Val
            22100             22105             22110
Glu Lys Thr Glu Tyr Glu Phe Arg Val Lys Ala Lys Asn Asp Ala Gly
    22115             22120             22125
Tyr Ser Glu Pro Arg Glu Ala Phe Ser Ser Val Ile Ile Lys Glu Pro
    22130             22135             22140                 2
Gln Ile Glu Pro Thr Ala Asp Leu Thr Gly Ile Thr Asn Gln Leu Ile
2145          22150             22155             22160
Thr Cys Lys Ala Gly Ser Pro Phe Thr Ile Asp Val Pro Ile Ser Gly
            22165             22170             22175
Arg Pro Ala Pro Lys Val Thr Trp Lys Leu Glu Glu Met Arg Leu Lys
    22180             22185             22190
Glu Thr Asp Arg Val Ser Ile Thr Thr Thr Lys Asp Arg Thr Thr Leu
    22195             22200             22205
Thr Val Lys Asp Ser Met Arg Gly Asp Ser Gly Arg Tyr Phe Leu Thr
    22210             22215             22220                 2
Leu Glu Asn Thr Ala Gly Val Lys Thr Phe Ser Val Thr Val Val Val
2225          22230             22235             22240
Ile Gly Arg Pro Gly Pro Val Thr Gly Pro Ile Glu Val Ser Ser Val
            22245             22250             22255
Ser Ala Glu Ser Cys Val Leu Ser Trp Gly Glu Pro Lys Asp Gly Gly
    22260             22265             22270
Gly Thr Glu Ile Thr Asn Tyr Ile Val Glu Lys Arg Glu Ser Gly Thr
    22275             22280             22285
Thr Ala Trp Gln Leu Val Asn Ser Ser Val Lys Arg Thr Gln Ile Lys
    22290             22295             22300                 2
Val Thr His Leu Thr Lys Tyr Met Glu Tyr Ser Phe Arg Val Ser Ser
2305          22310             22315             22320
Glu Asn Arg Phe Gly Val Ser Lys Pro Leu Glu Ser Ala Pro Ile Ile
            22325             22330             22335
Ala Glu His Pro Phe Val Pro Pro Ser Ala Pro Thr Arg Pro Glu Val
          22340             22345             22350
Tyr His Val Ser Ala Asn Ala Met Ser Ile Arg Trp Glu Glu Pro Tyr
    22355             22360             22365
His Asp Gly Gly Ser Lys Ile Ile Gly Tyr Trp Val Glu Lys Lys Glu
    22370             22375             22380                 2
Arg Asn Thr Ile Leu Trp Val Lys Glu Asn Lys Val Pro Cys Leu Glu
2385          22390             22395             22400
Cys Asn Tyr Lys Val Thr Gly Leu Val Glu Gly Leu Glu Tyr Gln Phe
            22405             22410             22415
Arg Thr Tyr Ala Leu Asn Ala Ala Gly Val Ser Lys Ala Ser Glu Ala
            22420             22425         22430
Ser Arg Pro Ile Met Ala Gln Asn Pro Val Asp Ala Pro Gly Arg Pro
    22435             22440             22445
Glu Val Thr Asp Val Thr Arg Ser Thr Val Ser Leu Ile Trp Ser Ala
    22450             22455             22460                 2
Pro Ala Tyr Asp Gly Gly Ser Lys Val Val Gly Tyr Ile Ile Glu Arg
2465          22470             22475             22480
Lys Pro Val Ser Glu Val Gly Asp Gly Arg Trp Leu Lys Cys Asn Tyr
            22485             22490             22495
Thr Ile Val Ser Asp Asn Phe Phe Thr Val Thr Ala Leu Ser Glu Gly
            22500             22505             22510
Asp Thr Tyr Glu Phe Arg Val Leu Ala Lys Asn Ala Ala Gly Val Ile
    22515             22520             22525
Ser Lys Gly Ser Glu Ser Thr Gly Pro Val Thr Cys Arg Asp Glu Tyr
    22530             22535             22540                 2
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Ala Pro Pro Lys Ala Glu Leu Asp Ala Arg Leu His Gly Asp Leu Val
2545            22550            22555            22560
Thr Ile Arg Ala Gly Ser Asp Leu Val Leu Asp Ala Ala Val Gly Gly
        22565            22570       ·     22575
Lys Pro Glu Pro Lys Ile Ile Trp Thr Lys Gly Asp Lys Glu Leu Asp
        22580            22585            22590
Leu Cys Glu Lys Val Ser Leu Gln Tyr Thr Gly Lys Arg Ala Thr Ala
    22595            22600            22605         ·
Val Ile Lys Phe Cys Asp Arg Ser Asp Ser Gly Lys Tyr Thr Leu Thr
    22610            22615            22620            2
Val Lys Asn Ala Ser Gly Thr Lys Ala Val Ser Val Met Val Lys Val
2625            22630            22635            22640
Leu Asp Ser Pro Gly Pro Cys Gly Lys Leu Thr Val Ser Arg Val Thr
        22645            22650            22655
Gln Glu Lys Cys Thr Leu Ala Trp Ser Leu Pro Gln Glu Asp Gly Gly
        22660            22665            22670
Ala Glu Ile Thr His Tyr Ile Val Glu Arg Arg Glu Thr Ser Arg Leu
    22675      ·      22680            22685
Asn Trp Val Ile Val Glu Gly Glu Cys Pro Thr Leu Ser Tyr Val Val
    22690            22695            22700            2
Thr Arg Leu Ile Lys.Asn Asn Glu Tyr Ile Phe Arg Val Arg Ala Val
2705            22710            22715            22720
Asn Lys Tyr Gly Pro Gly Val Pro Val Glu Ser Glu Pro Ile Val Ala
        22725            22730            22735
Arg Asn Ser Phe Thr Ile Pro Ser Pro Pro Gly Ile Pro Glu Glu Val
        22740            22745            22750
Gly Thr Gly Lys Glu His Ile Ile Ile Gln Trp Thr Lys Pro Glu Ser
    22755            22760            22765
Asp Gly Gly Asn Glu Ile Ser Asn Tyr Leu Val Asp Lys Arg Glu Lys
    22770            22775            22780            2
Glu Ser Leu Arg Trp Thr Arg Val Asn Lys Asp Tyr Val Val Tyr Asp
2785            22790            22795            22800
Thr Arg Leu Lys Val Thr Ser Leu Met Glu Gly Cys Asp Tyr Gln Phe
        22805            22810            22815
Arg Val Thr Ala Val Asn Ala Ala Gly Asn Ser Glu Pro Ser Glu Arg
        22820            22825    ·        22830
Ser Asn Phe Ile Ser Cys Arg Glu Pro Ser Tyr Thr Pro Gly Pro Pro
        22835            22840            22845
Ser Ala Pro Arg Val Val Asp Thr Thr Lys His Ser·Ile Ser Leu Ala
    22850            22855            22860            2
Trp Thr Lys Pro Met Tyr Asp Gly Gly Thr Asp Ile Val Gly Tyr Val
2865     ·      22870            22875            22880
Leu Glu Met·Gln Glu Lys Asp Thr Asp Gln Trp Tyr Arg Val His Thr
        22885            22890            22895
Asn Ala Thr Ile Arg Asn Thr Glu Phe Thr Val Pro Asp Leu Lys Met
        22900            22905            22910
Gly Gln Lys Tyr Ser Phe Arg Val Ala Ala Val Asn Val Lys Gly Met
        22915            22920            22925
Ser Glu Tyr Ser Glu Ser Ile Ala Glu Ile Glu Pro Val Glu Arg Ile
    22930            22935            22940            2
Glu Ile Pro Asp Leu Glu Leu Ala Asp Asp Leu Lys Lys Thr Val Thr
2945            22950            22955            22960
Ile Arg Ala Gly Ala Ser Leu Arg Leu Met Val Ser Val Ser Gly Arg
        22965            22970            22975
Pro Pro Pro Val Ile Thr Trp Ser Lys Gln Gly Ile Asp Leu Ala Ser
        22980            22985            22990
Arg Ala Ile Ile Asp Thr Thr Glu Ser Tyr Ser Leu Leu Ile Val Asp
        22995            23000            23005
Lys Val Asn Arg Tyr Asp Ala Gly Lys Tyr Thr Ile Glu Ala Glu Asn
    23010            23015            23020            2
Gln Ser Gly Lys Lys Ser Ala Thr Val Leu Val Lys Val Tyr Asp Thr
3025     ·      23030            23035            23040
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Pro Gly Pro Cys Pro Ser Val Lys Val Lys Glu Val Ser Arg Asp Ser
        23045              23050              23055
Val Thr Ile Thr Trp Glu Ile Pro Thr Ile Asp Gly Gly Ala Pro Ile
        23060              23065              23070
Asn Asn Tyr Ile Val Glu Lys Arg Glu Ala Ala Met Arg Ala Phe Lys
        23075              23080              23085
Thr Val Thr Thr Lys Cys Ser Lys Thr Leu Tyr Arg Ile Ser Gly Leu
   23090              23095              23100              2
Val Glu Gly Thr Met His Tyr Phe Arg Val Leu Pro Glu Asn Ile Tyr
3105              23110              23115              23120
Gly Ile Gly Glu Pro Cys Glu Thr Ser Asp Ala Val Leu Val Ser Glu
        23125              23130              23135
Val Pro Leu Val Pro Ala Lys Leu Glu Val Val Asp Val Thr Lys Ser
        23140              23145              23150
Thr Val Thr Leu Ala Trp Glu Lys Pro Leu Tyr Asp Gly Gly Ser Arg
        23155              23160              23165
Leu Thr Gly Tyr Val Leu Glu Ala Cys Lys Ala Gly Thr Glu Arg Trp
   23170              23175              23180              2
Met Lys Val Val Thr Leu Lys Pro Thr Val Leu Glu His Thr Val Thr
3185              23190              23195              23200
Ser Leu Asn Glu Gly Glu Gln Tyr Leu Phe Arg Ile Arg Ala Gln Asn
        23205              23210              23215
Glu Lys Gly Val Ser Glu Pro Arg Glu Thr Val Thr Ala Val Thr Val
        23220              23225              23230
Gln Asp Leu Arg Val Leu Pro Thr Ile Asp Leu Ser Thr Met Pro Gln
        23235              23240              23245
Lys Thr Ile His Val Pro Ala Gly Arg Pro Val Glu Leu Val Ile Pro
   23250              23255              23260              2
Ile Ala Gly Arg Pro Pro Pro Ala Ala Ser Trp Phe Phe Ala Gly Ser
3265              23270              23275              23280
Lys Leu Arg Glu Ser Glu Arg Val Thr Val Glu Thr His Thr Lys Val
        23285              23290              23295
Ala Lys Leu Thr Ile Arg Glu Thr Thr Ile Arg Asp Thr Gly Glu Tyr
        23300              23305              23310
Thr Leu Glu Leu Lys Asn Val Thr Gly Thr Thr Ser Glu Thr Ile Lys
        23315              23320              23325
Val Ile Ile Leu Asp Lys Pro Gly Pro Pro Thr Gly Pro Ile Lys Ile
   23330              23335              23340              2
Asp Glu Ile Asp Ala Thr Ser Ile Thr Ile Ser Trp Glu Pro Pro Glu
3345              23350              23355              23360
Leu Asp Gly Gly Ala Pro Leu Ser Gly Tyr Val Val Glu Gln Arg Asp
   .    23365              23370              23375
Ala His Arg Pro Gly Trp Leu Pro Val Ser Glu Ser Val Thr Arg Ser
        23380              23385              23390
Thr Phe Lys Phe Thr Arg Leu Thr Glu Gly Asn Glu Tyr Val Phe Arg
        23395              23400              23405
Val Ala Ala Thr Asn Arg Phe Gly Ile Gly Ser Tyr Leu Gln Ser Glu
   23410              23415              23420              2
Val Ile Glu Cys Arg Ser Ser Ile Arg Ile Pro Gly Pro Pro Glu Thr
3425              23430              23435              23440
Leu Gln Ile Phe Asp Val Ser Arg Asp Gly Met Thr Leu Thr Trp Tyr
        23445              23450              23455
Pro Pro Glu Asp Asp Gly Gly Ser Gln Val Thr Gly Tyr Ile Val Glu
        23460              23465              23470
Arg Lys Glu Val Arg Ala Asp Arg Trp Val Arg Val Asn Lys Val Pro
        23475              23480              23485
Val Thr Met Thr Arg Tyr Arg Ser Thr Gly Leu Thr Glu Gly Leu Glu
   23490              23495              23500              2
Tyr Glu His Arg Val Thr Ala Ile Asn Ala Arg Gly Ser Gly Lys Pro
3505              23510              23515              23520
Ser Arg Pro Ser Lys Pro Ile Val Ala Met Asp Pro Ile Ala Pro Pro
        23525              23530              23535
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Gly Lys Pro Gln Asn Pro Arg Val Thr Asp Thr Thr Arg Thr Ser Val
        23540                    23545                    23550
Ser Leu Ala Trp Ser Val Pro Glu Asp Glu Gly Gly Ser Lys Val Thr
        23555                23560                    23565
Gly Tyr Leu Ile Glu Met Gln Lys Val Asp Gln His Glu Trp Thr Lys
    23570                23575                23580                    2
Cys Asn Thr Thr Pro Thr Lys Ile Arg Glu Tyr Thr Leu Thr His Leu
3585                23590                23595                    23600
Pro Gln Gly Ala Glu Tyr Arg Phe Arg Val Leu Ala Cys Asn Ala Gly
            23605                23610                23615
Gly Pro Gly Glu Pro Ala Glu Val Pro Gly Thr Val Lys Val Thr Glu
        23620                23625                23630
Met Leu Glu Tyr Pro Asp Tyr Glu Leu Asp Glu Arg Tyr Gln Glu Gly
        23635                23640                23645
Ile Phe Val Arg Gln Gly Gly Val Ile Arg Leu Thr Ile Pro Ile Lys
    23650                23655                23660                    2
Gly Lys Pro Phe Pro Ile Cys Lys Trp Thr Lys Glu Gly Gln Asp Ile
3665                23670                23675                    23680
Ser Lys Arg Ala Met Ile Ala Thr Ser Glu Thr His Thr Glu Leu Val
            23685                23690                23695
Ile Lys Glu Ala Asp Arg Gly Asp Ser Gly Thr Tyr Asp Leu Val Leu
        23700                23705                23710
Glu Asn Lys Cys Gly Lys Lys Ala Val Tyr Ile Lys Val Arg Val Ile
        23715                23720                23725
Gly Ser Pro Asn Ser Pro Glu Gly Pro Leu Glu Tyr Asp Asp Ile Gln
    23730                23735                23740                    2
Val Arg Ser Val Arg Val Ser Trp Arg Pro Pro Ala Asp Asp Gly Gly
3745                23750                23755                    23760
Ala Asp Ile Leu Gly Tyr Ile Leu Glu Arg Arg Glu Val Pro Lys Ala
            23765                23770                23775
Ala Trp Tyr Thr Ile Asp Ser Arg Val Arg Gly Thr Ser Leu Val Val
        23780                23785                23790
Lys Gly Leu Lys Glu Asn Val Glu Tyr His Phe Arg Val Ser Ala Glu
        23795                23800                23805
Asn Gln Phe Gly Ile Ser Lys Pro Leu Lys Ser Glu Glu Pro Val Thr
    23810                23815                23820                    2
Pro Lys Thr Pro Leu Asn Pro Pro Glu Pro Pro Ser Asn Pro Pro Glu
3825                23830                23835                    23840
Val Leu Asp Val Thr Lys Ser Ser Val Ser Leu Ser Trp Ser Arg Pro
            23845                23850                23855
Lys Asp Asp Gly Gly Ser Arg Val Thr Gly Tyr Tyr Ile Glu Arg Lys
        23860                23865                23870
Glu Thr Ser Thr Asp Lys Trp Val Arg His Asn Lys Thr Gln Ile Thr
    23875                23880                23885
Thr Thr Met Tyr Thr Val Thr Gly Leu Val Pro Asp Ala Glu Tyr Gln
    23890                23895                23900                    2
Phe Arg Ile Ile Ala Gln Asn Asp Val Gly Leu Ser Glu Thr Ser Pro
3905                23910                23915                    23920
Ala Ser Glu Pro Val Val Cys Lys Asp Pro Phe Asp Lys Pro Ser Gln
            23925        .        23930                23935
Pro Gly Glu Leu Glu Ile Leu Ser Ile Ser Lys Asp Ser Val Thr Leu
        23940                23945                23950
Gln Trp Glu Lys Pro Glu Cys Asp Gly Gly Lys Glu Ile Leu Gly Tyr
        23955                23960                23965
Trp Val Glu Tyr Arg Gln Ser Gly Asp Ser Ala Trp Lys Lys Ser Asn
    23970                23975                23980                    2
Lys Glu Arg Ile Lys Asp Lys Gln Phe Thr Ile Gly Gly Leu Leu Glu
3985                23990                23995                    24000
Ala Thr Glu Tyr Glu Phe Arg Val Phe Ala Glu Asn Glu Thr Gly Leu
            24005                24010                24015
Ser Arg Pro Arg Arg Thr Ala Met Ser Ile Lys Thr Lys Leu Thr Ser
        24020                24025                24030
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Gly Glu Ala Pro Gly Ile Arg Lys Glu Met Lys Asp Val Thr Thr Lys
     24035                 24040                 24045
Leu Gly Glu Ala Ala Gln Leu Ser Cys Gln Ile Val Gly Arg Pro Leu
     24050                 24055                 24060          2
Pro Asp Ile Lys Trp Tyr Arg Phe Gly Lys Glu Leu Ile Gln Ser Arg
 4065                 24070                 24075                 24080
Lys Tyr Lys Met Ser Ser Asp Gly Arg Thr His Thr Leu Thr Val Met
     24085                 24090                 24095
Thr Glu Glu Gln Glu Asp Glu Gly Val Tyr Thr Cys Ile Ala Thr Asn
     24100                 24105                 24110
Glu Val Gly Glu Val Glu Thr Ser Ser Lys Leu Leu Leu Gln Ala Thr
     24115                 24120                 24125
Pro Gln Phe His Pro Gly Tyr Pro Leu Lys Glu Lys Tyr Tyr Gly Ala
     24130                 24135                 24140          2
Val Gly Ser Thr Leu Arg Leu His Val Met Tyr Ile Gly Arg Pro Val
 4145                 24150                 24155                 24160
Pro Ala Met Thr Trp Phe His Gly Gln Lys Leu Leu Gln Asn Ser Glu
     24165                 24170                 24175
Asn Ile Thr Ile Glu Asn Thr Glu His Tyr Thr His Leu Val Met Lys
     24180                 24185                 24190
Asn Val Gln Arg Lys Thr His Ala Gly Lys Tyr Lys Val Gln Leu Ser
     24195                 24200                 24205
Asn Val Phe Gly Thr Val Asp Ala Ile Leu Asp Val Glu Ile Gln Asp
     24210                 24215                 24220          2
Lys Pro Asp Lys Pro Thr Gly Pro Ile Val Ile Glu Ala Leu Leu Lys
 4225                 24230                 24235                 24240
Asn Ser Ala Val Ile Ser Trp Lys Pro Pro Ala Asp Asp Gly Gly Ser
     24245                 24250                 24255
Trp Ile Thr Asn Tyr Val Val Glu Lys Cys Glu Ala Lys Glu Gly Ala
     24260                 24265                 24270
Glu Trp Gln Leu Val Ser Ser Ala Ile Ser Val Thr Thr Cys Arg Ile
     24275                 24280                 24285
Val Asn Leu Thr Glu Asn Ala Gly Tyr Tyr Phe Arg Val Ser Ala Gln
     24290                 24295                 24300          2
Asn Thr Phe Gly Ile Ser Asp Pro Leu Glu Val Ser Ser Val Val Ile
 4305                 24310                 24315                 24320
Ile Lys Ser Pro Phe Glu Lys Pro Gly Ala Pro Gly Lys Pro Thr Ile
     24325                 24330                 24335
Thr Ala Val Thr Lys Asp Ser Cys Val Val Ala Trp Lys Pro Pro Ala
     24340                 24345                 24350
Ser Asp Gly Gly Ala Lys Ile Arg Asn Tyr Tyr Leu Glu Lys Arg Glu
    ·24355                 24360                 24365
Lys Lys Gln Asn Lys Trp Ile Ser Val Thr Thr Glu Glu Ile Arg Glu
     24370                 24375                 24380          2
Thr Val Phe Ser Val Lys Asn Leu Ile Glu Gly Leu Glu Tyr Glu Phe
 4385                 24390                 24395                 24400
Arg Val Lys Cys Glu Asn Leu Gly Gly Glu Ser Glu Trp Ser Glu Ile
     24405                 24410                 24415
Ser Glu Pro Ile Thr Pro Lys Ser Asp Val Pro Ile Gln Ala Pro His
     24420                 24425                 24430
Phe Lys Glu Glu Leu Arg Asn Leu Asn Val Arg Tyr Gln Ser Asn Ala
     24435                 24440                 24445
Thr Leu Val Cys Lys Val Thr Gly His Pro Lys Pro Ile Val Lys Trp
     24450                 24455                 24460          2
Tyr Arg Gln Gly Lys Glu Ile Ile Ala Asp Gly Leu Lys Tyr Arg Ile
 4465                 24470                 24475                 24480
Gln Glu Phe Lys Gly Gly Tyr His Gln Leu Ile Ile Ala Ser Val Thr
     24485                 24490                 24495
Asp Asp Asp Ala Thr Val Tyr Gln Val Arg Ala Thr Asn Gln Gly Gly
     24500                 24505                 24510
Ser Val Ser Gly Thr Ala Ser Leu Glu Val Glu Val Pro Ala Lys Ile
     24515                 24520                 24525
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His Leu Pro Lys Thr Leu Glu Gly Met Gly Ala Val His Ala Leu Arg
   24530   24535   24540   2
Gly Glu Val Val Ser Ile Lys Ile Pro Phe Ser Gly Lys Pro Asp Pro
4545   24550   24555   24560
Val Ile Thr Trp Gln Lys Gly Gln Asp Leu Ile Asp Asn Asn Gly His
                24565   24570   24575
Tyr Gln Val Ile Val Thr Arg Ser Phe Thr Ser Leu Val Phe Pro Asn
                24580   24585   24590
Gly Val Glu Arg Lys Asp Ala Gly Phe Tyr Val Val Cys Ala Lys Asn
                24595   24600   24605
Arg Phe Gly Ile Asp Gln Lys Thr Val Glu Leu Asp Val Ala Asp Val
   24610   24615   24620   2
Pro Asp Pro Pro Arg Gly Val Lys Val Ser Asp Ala Ser Arg Asp Ser
4625   24630   24635   24640
Val Asn Leu Thr Trp Thr Glu Pro Ala Ser Asp Gly Gly Ser Lys Ile
                24645   24650   24655
Thr Asn Tyr Ile Val Glu Lys Cys Ala Thr Thr Ala Glu Arg Trp Leu
                24660   24665   24670
Arg Val Gly Gln Ala Arg Glu Thr Arg Tyr Thr Val Ile Asn Leu Phe
   24675   24680   24685
Gly Lys Thr Ser Tyr Gln Phe Arg Val Ile Ala Glu Asn Lys Phe Gly
   24690   24695   24700   2
Leu Ser Lys Pro Ser Glu Pro Ser Glu Pro Thr Ile Thr Lys Glu Asp
4705   24710   24715   24720
Lys Thr Arg Ala Met Asn Tyr Asp Glu Glu Val Asp Glu Thr Arg Glu
                24725   24730   24735
Val Ser Met Thr Lys Ala Ser His Ser Ser Thr Lys Glu Leu Tyr Glu
                24740   24745   24750
Lys Tyr Met Ile Ala Glu Asp Leu Gly Arg Gly Glu Phe Gly Ile Val
   24755   24760   24765
His Arg Cys Val Glu Thr Ser Ser Lys Lys Thr Tyr Met Ala Lys Phe
   24770   24775   24780   2
Val Lys Val Lys Gly Thr Asp Gln Val Leu Val Lys Lys Glu Ile Ser
4785   24790   24795   24800
Ile Leu Asn Ile Ala Arg His Arg Asn Ile Leu His Leu His Glu Ser
                24805   24810   24815
Phe Glu Ser Met Glu Glu Leu Val Met Ile Phe Glu Phe Ile Ser Gly
                24820   24825   24830
Leu Asp Ile Phe Glu Arg Ile Asn Thr Ser Ala Phe Glu Leu Asn Glu
   24835   24840   24845
Arg Glu Ile Val Ser Tyr Val His Gln Val Cys Glu Ala Leu Gln Phe
   24850   24855   24860   2
Leu His Ser His Asn Ile Gly His Phe Asp Ile Arg Pro Glu Asn Ile
4865   24870   24875   24880
Ile Tyr Gln Thr Arg Arg Ser Ser Thr Ile Lys Ile Ile Glu Phe Gly
                24885   24890   24895
Gln Ala Arg Gln Leu Lys Pro Gly Asp Asn Phe Arg Leu Leu Phe Thr
   24900   24905   24910
Ala Pro Glu Tyr Tyr Ala Pro Glu Val His Gln His Asp Val Val Ser
   24915   24920   24925
Thr Ala Thr Asp Met Trp Ser Leu Gly Thr Leu Val Tyr Val Leu Leu
   24930   24935   24940   2
Ser Gly Ile Asn Pro Phe Leu Ala Glu Thr Asn Gln Gln Ile Ile Glu
4945   24950   24955   24960
Asn Ile Met Asn Ala Glu Tyr Thr Phe Asp Glu Glu Ala Phe Lys Glu
                24965   24970   24975
Ile Ser Ile Glu Ala Met Asp Phe Val Asp Arg Leu Leu Val Lys Glu
   24980   24985   24990
Arg Lys Ser Arg Met Thr Ala Ser Glu Ala Leu Gln His Pro Trp Leu
   24995   25000   25005
Lys Gln Lys Ile Glu Arg Val Ser Thr Lys Val Ile Arg Thr Leu Lys
   25010   25015   25020   2

His Arg Arg Tyr Tyr His Thr Leu Ile Lys Lys Asp Leu Asn Met Val
5025   25030   25035   25040
Val Ser Ala Ala Arg Ile Ser Cys Gly Gly Ala Ile Arg Ser Gln Lys
        25045   25050   25055
Gly Val Ser Val Ala Lys Val Lys Val Ala Ser Ile Glu Ile Gly Pro
        25060   25065   25070
Val Ser Gly Gln Ile Met His Ala Val Gly Glu Glu Gly Gly His Val
    25075   25080   25085
Lys Tyr Val Cys Lys Ile Glu Asn Tyr Asp Gln Ser Thr Gln Val Thr
    25090   25095   25100   2
Trp Tyr Phe Gly Val Arg Gln Leu Glu Asn Ser Glu Lys Tyr Glu Ile
5105   25110   25115   25120
Thr Tyr Glu Asp Gly Val Ala Ile Leu Tyr Val Lys Asp Ile Thr Lys
        25125   25130   25135
Leu Asp Asp Gly Thr Tyr Arg Cys Lys Val Val Asn Asp Tyr Gly Glu
        25140   25145   25150
Asp Ser Ser Tyr Ala Glu Leu Phe Val Lys Gly Val Arg Glu Val Tyr
    25155   25160   25165
Asp Tyr Tyr Cys Arg Arg Thr Met Lys Lys Ile Lys Arg Arg Thr Asp
    25170   25175   25180   2
Thr Met Arg Leu Leu Glu Arg Pro Pro Glu Thr Leu Pro Leu Tyr
5185   25190   25195   25200
Asn Lys Thr Ala Tyr Val Gly Glu Asn Val Arg Phe Gly Val Thr Ile
        25205   25210   25215
Thr Val His Pro Glu Pro His Val Thr Trp Tyr Lys Ser Gly Gln Lys
        25220   25225   25230
Ile Lys Pro Gly Asp Asn Asp Lys Lys Tyr Thr Phe Glu Ser Asp Lys
    25235   25240   25245
Gly Leu Tyr Gln Leu Thr Ile Asn Ser Val Thr Thr Asp Asp Asp Ala
    25250   25255   25260   2
Glu Tyr Thr Val Val Ala Arg Asn Lys Tyr Gly Glu Asp Ser Cys Lys
5265   25270   25275   25280
Ala Lys Leu Thr Val Thr Leu His Pro Pro Pro Thr Asp Ser Thr Leu
        25285   25290   25295
Arg Pro Met Phe Lys Arg Leu Leu Ala Asn Ala Glu Cys Gln Glu Gly
        25300   25305   25310
Gln Ser Val Cys Phe Glu Ile Arg Val Ser Gly Ile Pro Pro Pro Thr
        25315   25320   25325
Leu Lys Trp Glu Lys Asp Gly Gln Pro Leu Ser Leu Gly Pro Asn Ile
    25330   25335   25340   2
Glu Ile Ile His Glu Gly Leu Asp Tyr Tyr Ala Leu His Ile Arg Asp
5345   25350   25355   25360
Thr Leu Pro Glu Asp Thr Gly Tyr Tyr Arg Val Thr Ala Thr Asn Thr
        25365   25370   25375
Ala Gly Ser Thr Ser Cys Gln Ala His Leu Gln Val Glu Arg Leu Arg
        25380   25385   25390
Tyr Lys Lys Gln Glu Phe Lys Ser Lys Glu Glu His Glu Arg His Val
    25395   25400   25405
Gln Lys Gln Ile Asp Lys Thr Leu Arg Met Ala Glu Ile Leu Ser Gly
    25410   25415   25420   2
Thr Glu Ser Val Pro Leu Thr Gln Val Ala Lys Glu Ala Leu Arg Glu
5425   25430   25435   25440
Ala Ala Val Leu Tyr Lys Pro Ala Val Ser Thr Lys Thr Val Lys Gly
        25445   25450   25455
Glu Phe Arg Leu Glu Ile Glu Glu Lys Lys Glu Glu Arg Lys Leu Arg
        25460   25465   25470
Met Pro Tyr Asp Val Pro Glu Pro Arg Lys Tyr Lys Gln Thr Thr Ile
    25475   25480   25485
Glu Glu Asp Gln Arg Ile Lys Gln Phe Val Pro Met Ser Asp Met Lys
    25490   25495   25500   2
Trp Tyr Lys Lys Ile Arg Asp Gln Tyr Glu Met Pro Gly Lys Leu Asp
5505   25510   25515   25520

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Arg Val Val Gln Lys Arg Pro Lys Arg Ile Arg Leu Ser Arg Trp Glu
         25525               25530                   25535
Gln Phe Tyr Val Met Pro Leu Pro Arg Ile Thr Asp Gln Tyr Arg Pro
         25540               25545           ·    25550
Lys Trp Arg Ile Pro Lys Leu Ser Gln Asp Asp Leu Glu Ile Val Arg
         25555               25560               25565
Pro Ala Arg Arg Arg Thr Pro Ser Pro Asp Tyr Asp Phe Tyr Tyr Arg
    25570           25575               25580                   2
Pro Arg Arg Arg Ser Leu Gly Asp Ile Ser Asp Glu Glu Leu Leu Leu
5585           25590               25595                   25600
Pro Ile Asp Asp Tyr Leu Ala Met Lys Arg Thr Glu Glu Glu Arg Leu
         25605               25610               25615
Arg Leu Glu Glu Glu Leu Glu Leu Gly Phe Ser Ala Ser Pro Pro Ser
         25620               25625               25630
Arg Ser Pro Pro His Phe Glu Leu Ser Ser Leu Arg Tyr Ser Ser Pro
    25635               25640               25645
Gln Ala His Val Lys Val Glu Glu Thr Arg Lys Asn Phe Arg Tyr Ser
    25650               25655               25660                   2
Thr Tyr His Ile Pro Thr Lys Ala Glu Ala Ser Thr Ser Tyr Ala Glu
5665           25670               25675               25680
Leu Arg Glu Arg His Ala Gln Ala Ala Tyr Arg Gln Pro Lys Gln Arg
         25685               25690               25695
Gln Arg Ile Met Ala Glu Arg Glu Asp Glu Glu Leu Leu Arg Pro Val
         25700               25705               25710  .
Thr Thr Thr Gln His Leu Ser Glu Tyr Lys Ser Glu Leu Asp Phe Met
    25715               25720               25725
Ser Lys Glu Glu Lys Ser Arg Lys Lys Ser Arg Arg Gln Arg Glu Val
    25730           25735               25740                   2
Thr Glu Ile Thr Glu Ile Glu Glu Tyr Glu Ile Ser Lys His Ala
5745           25750               25755               25760
Gln Arg Glu Ser Ser Ser Ser Ala Ser Arg Leu Leu Arg Arg Arg Arg
         25765               25770               25775
Ser Leu Ser Pro Thr Tyr Ile Glu Leu Met Arg Pro Val Ser Glu Leu
         25780               25785               25790
Ile Arg Ser Arg Pro Gln Pro Ala Glu Glu Tyr Glu Asp Asp Thr Glu
    25795               25800           .     25805
Arg Arg Ser Pro Thr Pro Glu Arg Thr Arg Pro Arg Ser Pro Ser Pro
    25810               25815               25820                   2
Val Ser Ser Glu Arg Ser Leu Ser Arg Phe Glu Arg Ser Ala Arg Phe
5825               25830               25835               25840
Asp Ile Phe Ser Arg Tyr Glu Ser Met Lys Ala Ala Leu Lys Thr Gln
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Lys Thr Ser Glu Arg Lys Tyr Glu Val Leu Ser Gln Gln Pro Phe Thr
         25860               25865               25870
Leu Asp His Ala Pro Arg Ile Thr Leu Arg Met Arg Ser His Arg Val
    25875           ·    25880               25885
Pro Cys Gly Gln Asn Thr Arg Phe Ile Leu Asn Val Gln Ser Lys Pro
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Thr Ala Glu Val Lys Trp Tyr His Asn Gly Val Glu Leu Gln Glu Ser
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Ser Lys Ile His Tyr Thr Asn Thr Ser Gly Val Leu Thr Leu Glu Ile
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Leu Asp Cys His Thr Asp Asp Ser Gly Thr Tyr Arg Ala Val Cys Thr
         25940               25945               25950
Asn Tyr Lys Gly Glu Ala Ser Asp Tyr Ala Thr Leu Asp Val Thr Gly
    25955               25960               25965
Gly Asp Tyr Thr Thr Tyr Ala Ser Gln Arg Arg Asp Glu Glu Val Pro
    25970               25975               25980                   2
Arg Ser Val Phe Pro Glu Leu Thr Arg Thr Glu Ala Tyr Ala Val Pro
5985               25990               25995               26000
Ser Phe Lys Lys Thr Ser Glu Met Glu Ala Ser Ser Ser Val Arg Glu
         26005               26010               26015
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Val Lys Ser Gln Met Thr Glu Thr Arg Glu Ser Leu Ser Ser Tyr Glu
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His Ser Ala Ser Ala Glu Met Lys Ser Ala Ala Leu Glu Glu Lys Ser
         26035                26040                26045
Leu Glu Glu Lys Ser Thr Thr Arg Lys Ile Lys Thr Thr Leu Ala Ala
         26050                26055                26060         2
Arg Ile Leu Thr Lys Pro Arg Ser Met Thr Val Tyr Glu Gly Glu Ser
6065          26070                26075                26080
Ala Arg Phe Ser Cys Asp Thr Asp Gly Glu Pro Val Pro Thr Val Thr
         26085                26090                26095
Trp Leu Arg Lys Gly Gln Val Leu Ser Thr Ser Ala Arg His Gln Val
         26100                26105                26110
Thr Thr Thr Lys Tyr Lys Ser Thr Phe Glu Ile Ser Ser Val Gln Ala
         26115                26120                26125
Ser Asp Glu Gly Asn Tyr Ser Val Val Val Glu Asn Ser Glu Gly Lys
         26130                26135                26140         2
Gln Glu Ala Glu Phe Thr Leu Thr Ile Gln Lys Ala Arg Val Thr Glu
6145          26150                26155                26160
Lys Ala Val Thr Ser Pro Pro Arg Val Lys Ser Pro Glu Pro Arg Val
         26165                26170                26175
Lys Ser Pro Glu Ala Val Lys Ser Pro Lys Arg Val Lys Ser Pro Glu
         26180                26185                26190
Pro Ser His Pro Lys Ala Val Ser Pro Thr Glu Thr Lys Pro Thr Pro
         26195                26200                26205
Arg Glu Lys Val Gln His Leu Pro Val Ser Ala Pro Pro Lys Ile Thr
6210          26215                26220                       2
Gln Phe Leu Lys Ala Glu Ala Ser Lys Glu Ile Ala Lys Leu Thr Cys
6225          26230                26235                26240
Val Val Glu Ser Ser Val Leu Arg Ala Lys Glu Val Thr Trp Tyr Lys
         26245                26250          ·     26255
Asp Gly Lys Lys Leu Lys Glu Asn Gly His Phe Gln Phe His Tyr Ser
         26260                26265                26270
Ala Asp Gly Thr Tyr Glu Leu Lys Ile Asn Asn Leu Thr Glu Ser Asp
         26275                26280                26285
Gln Gly Glu Tyr Val Cys Glu Ile Ser Gly Glu Gly Gly Thr Ser Lys
         26290                26295                26300         2
Thr Asn Leu Gln Phe Met Gly Gln Ala Phe Lys Ser Ile His Glu Lys
6305          26310                26315                26320
Val Ser Lys Ile Ser Glu Thr Lys Lys Ser Asp Gln Lys Thr Thr Glu
         26325                26330                26335
Ser Thr Val Thr Arg Lys Thr Glu Pro Lys Ala Pro Glu Pro Ile Ser
         26340                26345                26350  ·
Ser Lys Pro Val Ile Val Thr Gly Leu Gln Asp Thr Thr Val Ser Ser
         26355                26360                26365
Asp Ser Val Ala Lys Phe Ala Val Lys Ala Thr Gly Glu Pro Arg Pro
         26370                26375                26380         2
Thr Ala Ile Trp Thr Lys Asp Gly Lys Ala Ile Thr Gln Gly Gly Lys
6385          26390                26395                26400
Tyr Lys Leu Ser Glu Asp Lys Gly Gly Phe Phe Leu Glu Ile His Lys
         26405          .     26410                26415
Thr Asp Thr Ser Asp Ser Gly Leu Tyr Thr Cys Thr Val Lys Asn Ser
         26420                26425                26430
Ala Gly Ser Val Ser Ser Ser Cys Lys Leu Thr Ile Lys Ala Ile Lys
         26435                26440                26445  ·
Asp Thr Glu Ala Gln Lys Val Ser Thr Gln Lys Thr Ser Glu Ile Thr
         26450                26455                26460         2
Pro Gln Lys Lys Ala Val Val Gln Glu Glu Ile Ser Gln Lys Ala Leu
6465          26470                26475                26480
Arg Ser Glu Glu Ile Lys Met Ser Glu Ala Lys Ser Gln Glu Lys Leu
         26485                26490                26495
Ala Leu Lys Glu Glu Ala Ser Lys Val Leu Ile Ser Glu Glu Val Lys
         26500                26505                26510
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Lys Ser Ala Ala Thr Ser Leu Glu Lys Ser Ile Val His Glu Glu Ile
      26515                 26520                 26525
Thr Lys Thr Ser Gln Ala Ser Glu Glu Val Arg Thr His Ala Glu Ile
      26530                 26535                 26540           2
Lys Ala Phe Ser Thr Gln Met Ser Ile Asn Glu Gly Gln Arg Leu Val
6545                  26550                 26555                 26560
Leu Lys Ala Asn Ile Ala Gly Ala Thr Asp Val Lys Trp Val Leu Asn
      26565                 26570                 26575
Gly Val Glu Leu Thr Asn Ser Glu Glu Tyr Arg Tyr Gly Val Ser Gly
          26580                 26585                 26590
Ser Asp Gln Thr Leu Thr Ile Lys Gln Ala Ser His Arg Asp Glu Gly
      26595                 26600                 26605
Ile Leu Thr Cys Ile Ser Lys Thr Lys Glu Gly Ile Val Lys Cys Gln
      26610                 26615                 26620           2
Tyr Asp Leu Thr Leu Ser Lys Glu Leu Ser Asp Ala Pro Ala Phe Ile
6625                  26630                 26635                 26640
Ser Gln Pro Arg Ser Gln Asn Ile Asn Glu Gly Gln Asn Val Leu Phe
          26645                 26650                 26655
Thr Cys Glu Ile Ser Gly Glu Pro Ser Pro Glu Ile Glu Trp Phe Lys
      26660                 26665                 26670
Asn Asn Leu Pro Ile Ser Ile Ser Ser Asn Val Ser Ile Ser Arg Ser
      26675                 26680                 26685
Arg Asn Val Tyr Ser Leu Glu Ile Arg Asn Ala Ser Val Ser Asp Ser
      26690                 26695                 26700           2
Gly Lys Tyr Thr Ile Lys Ala Lys Asn Phe Arg Gly Gln Cys Ser Ala
6705                  26710                 26715                 26720
Thr Ala Ser Leu Met Val Leu Pro Leu Val Glu Glu Pro Ser Arg Glu
          26725                 26730                 26735
Val Val Leu Arg Thr Ser Gly Asp Thr Ser Leu Gln Gly Ser Phe Ser
          26740                 26745                 26750
Ser Gln Ser Val Gln Met Ser Ala Ser Lys Gln Glu Ala Ser Phe Ser
      26755                 26760                 26765
Ser Phe Ser Ser Ser Ser Ala Ser Ser Met Thr Glu Met Lys Phe Ala
      26770                 26775                 26780           2
Ser Met Ser Ala Gln Ser Met Ser Ser Met Gln Glu Ser Phe Val Glu
6785                  26790                 26795                 26800
Met Ser Ser Ser Ser Phe Met Gly Ile Ser Asn Met Thr Gln Leu Glu
          26805                 26810                 26815
Ser Ser Thr Ser Lys Met Leu Lys Ala Gly Ile Arg Gly Ile Pro Pro
          26820                 26825                 26830
Lys Ile Glu Ala Leu Pro Ser Asp Ile Ser Ile Asp Glu Gly Lys Val
      26835                 26840                 26845
Leu Thr Val Ala Cys Ala Phe Thr Gly Glu Pro Thr Pro Glu Val Thr
      26850                 26855                 26860           2
Trp Ser Cys Gly Gly Arg Lys Ile His Ser Gln Glu Gln Gly Arg Phe
6865                  26870                 26875                 26880
His Ile Glu Asn Thr Asp Asp Leu Thr Thr Leu Ile Ile Met Asp Val
          26885                 26890                 26895
Gln Lys Gln Asp Gly Gly Leu Tyr Thr Leu Ser Leu Gly Asn Glu Phe
          26900                 26905                 26910
Gly Ser Asp Ser Ala Thr Val Asn Ile His Ile Arg Ser Ile
      26915                 26920                 26925
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